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BRITISH MEDICAL JOURNAL

LONDON SATURDAY FEBRUARY 3 1951

THE REACTIONS OF BACTERIA TO CHEMOTHERAPEUTIC AGENTS*

BY

LAWRENCE P. GARROD, M.D., F.R.C.P.

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Some of my predecessors in this lectureship have been able to choose subjects for it in which the late E. H. Kettle was himself interested. I have not been able to do this, and my subject is in fact one which was only just beginning to develop at the time of his death in 1936. If he had survived to see the remarkable changes which have taken place in medicine during the past 15 years, it would have been interesting to hear his comments on them. He had one of the most penetrating intellects of his time, and could grasp a subject in all its bearings when others saw only the surface of it. Those of us who were privileged to be his colleagues owe a good deal in our attitude to our subject, and even some of our opinions and beliefs, to what we learned from him in ordinary daily conversation. It was largely in this simple way that he exerted his influence and trained his colleagues, and for them it was a most agreeable process, because his comments on men and things were often highly entertaining as well as the product of a profound and original mind.

I have asked myself what his attitude would have been to advances in therapeutics which now make it possible to cure most bacterial infections. While I am sure that he would have welcomed them as everyone else has, I think it might have been with a tinge of regret that the conquest of this type of disease has come in just this way, without any addition to our knowledge of the process of infection and of the factors determining its onset and course. Some fundamental discovery in the field of immunity, could it have had the same practical results, would have been intellectually more satisfying.

Bacteria react in four ways to contact with chemotherapeutic drugs. These reactions may be described shortly as suppression, habituation, dependence, and stimulation. The first of these is best described by the general term "suppression," because it occurs in two forms: the effect may be directly lethal or it may involve simply the inhibition of further growth. This reaction is the aim of treatment, and will normally follow if the latter has been properly directed. The second, habituation or acquired resistance, is a path of escape from the suppressive influence of the drug which has been discovered by some species, often with inconvenient and even disastrous results.

*The Kettle Memorial Lecture, delivered at St. Bartholomew's Hospital Medical College on November 22, 1950.

Acquired Resistance to Sulphonamides

It is interesting to speculate on where we should stand now if the sulphonamides had remained our only resource in treating bacterial infections. There is no doubt that almost all species can become resistant to these drugs and that resistance to one drug involves resistance to all others. Its mechanism is known to be the formation by the organism of a sulphonamide inhibitor, shown in some cases to be *p*-aminobenzoic acid itself (MacLeod, 1940; Mirick, 1942; Landy *et al.*, 1943; Landy and Gerstung, 1944). On the other hand, this change occurs much more readily in some species than in others.

The first organism in which resistance was observed was the gonococcus: indeed, from the very inception of sulphanilamide treatment for gonorrhoea in 1936 a few cases failed to respond, and it is interesting that some resistant strains were found among 50 cultures isolated before this treatment had been introduced (Schmith and Reymann, 1940). These originally resistant strains naturally became increasingly prevalent, and the proportion of treatment failures steadily increased, especially during the war, reaching such figures as 50% (Campbell, 1944), 77% (Abrahamson, 1945), and 85.8% (Dunlop, 1949). There is ample proof that clinically resistant disease is due to strains demonstrably drug-resistant *in vitro* (Petro, 1943). Mahoney and Van Slyke (1945) went so far as to inoculate male volunteers with sensitive and resistant cultures in order to prove that their behaviour in the body would be the same.

It is surprising and very fortunate that the closely related meningococcus has behaved so differently. Sulphonamides are used in the treatment of cerebrospinal fever with the same success as at the time of their introduction 14 years ago: in fact, this is the only acute bacterial infection for which they still are used in preference to penicillin. If resistant strains of meningococcus were to appear they would surely have done so during mass sulphadiazine prophylaxis in the American armed Forces, which had such disastrous results in other directions; but Schoenbach and Phair (1948), who examined many strains isolated during this period, found none

unduly resistant, and no clear evidence even of a tendency to diminishing sensitivity.

The two most important sulphonamide-sensitive species—the pneumococcus and the haemolytic streptococcus—have behaved in a way intermediate between these extremes. Resistant strains of each have appeared, but they have not been common: how common they might be to-day but for the advent of penicillin no one can say. Resistance was observed in the pneumococcus comparatively early, and it seems that of these two organisms it has much the greater tendency to undergo this change. That pneumococci can be habituated to sulphapyridine without loss of virulence was first shown by MacLean, Rogers, and Fleming (1939); that such habituation may occur in patients treated for pneumonia and other conditions was shown by several groups of workers in the United States (e.g., Lowell *et al.*, 1940) during the early part of the war. It was also shown by Julianelle and Siegel (1945), in a very careful study, that mass sulphadiazine prophylaxis can produce a high prevalence of strains of pneumococci of progressively increasing resistance. It is quite possible that, but for the antibiotics, our main resource in the treatment of pneumonia would again be serum.

Haemolytic streptococci, the earliest object of sulphonamide attack, were long in betraying their capacity to develop resistance to it. This has been observed in only a few of the Griffith types of *Streptococcus pyogenes*, notably XII, XVII, and XIX, and their occurrence suggests dissemination from a few original foci rather than widespread habituation in treated individuals. They were first identified as causing cross-infection in wards where wounds and burns were under treatment (Francis, 1942). Much their widest sphere of activity was in the American armed Forces, in which hundreds of thousands of men were given 1 g. of sulphadiazine daily, mainly with the object of preventing haemolytic streptococcus infections. This treatment at first succeeded, but later highly resistant strains appeared and became widely prevalent (Epidemiology Unit 22, 1945; Damrosch, 1946), the last state of the units concerned being thus considerably worse than the first. Of the present distribution and frequency of such strains we have no information at all.

Acquired Resistance to Penicillin

There is one strong point of resemblance between sulphonamide-resistance and penicillin-resistance: the major difficulty occasioned by each is in infection by a single species—the gonococcus and *Staphylococcus pyogenes* respectively. Moreover, in each case selection and not adaptation is the mechanism by which resistant strains have become prevalent. The arguments supporting this view in connexion with staphylococci have been well expressed by Barber (Barber, 1947; Barber and Rozwadowska-Dowzenko, 1948; Barber et al., 1949), who is also responsible for much of our knowledge of the high prevalence of resistant strains in hospitals. Owing to cross-infection and the frequency of the carrier state in nurses, a single resistant strain of a particular phage type, often 52A, may achieve overwhelming predominance and cause serious trouble. On the other hand, in the population as a whole resistant strains are not yet so common: the proportion causing infections in outpatients in two London hospitals have recently been found to be 12.5% (Forbes, 1949) and 6.6% (Griffiths et al., 1949).

It is often asked whether infections due to these resistant staphylococci are amenable to treatment with penicillin given in very large doses. The answer may be found in the work of Gilson and Parker (1948), who showed that the amount of penicillinase formed by these organisms varies nearly a thousandfold. It is on the formation of this enzyme that their resistance depends: hence, presumably, clinical resistance must vary correspondingly, and strains forming the larger amounts must be uninfluenced by any concentration of the drug attainable in the body.

Resistance to penicillin in other species presents no such problem as this. It is of two kinds, one being a purely artificial condition produced in the laboratory, with no apparent counterpart in clinical infection. Thus Miller and Bohnhoff (1945, 1947a) have raised the resistance of both gonococci and meningococci to prodigious levels, but no such organism has ever been recovered from a treated patient. Haemolytic streptococci of Groups B and C can be made somewhat more resistant *in vitro* (Gezon, 1948), as can pneumococci both *in vitro* and in mice (Sesler and Schmidt, 1942; Eriksen, 1945), but there is no suggestion that such strains are being encountered in patients. Haemolytic streptococci of Group A are incapable of developing resistance, and there is fortunately no evidence that *Treponema pallidum* can do so.

These encouraging facts have led some authorities to contest the common belief that the widespread use of penicillin, often in inadequate doses, must eventually produce strains of bacteria other than staphylococci which are resistant to the drug. It is true that no such change has yet been shown to be in progress: indeed, the studies of Finland and his colleagues (Jackson *et al.*, 1950), who compared the sensitivity of 88 strains isolated before and 100 well after the introduction of penicillin, afford satisfying proof that this is not happening among pneumococci. It nevertheless remains a fact that some organisms do become more resistant in the body during

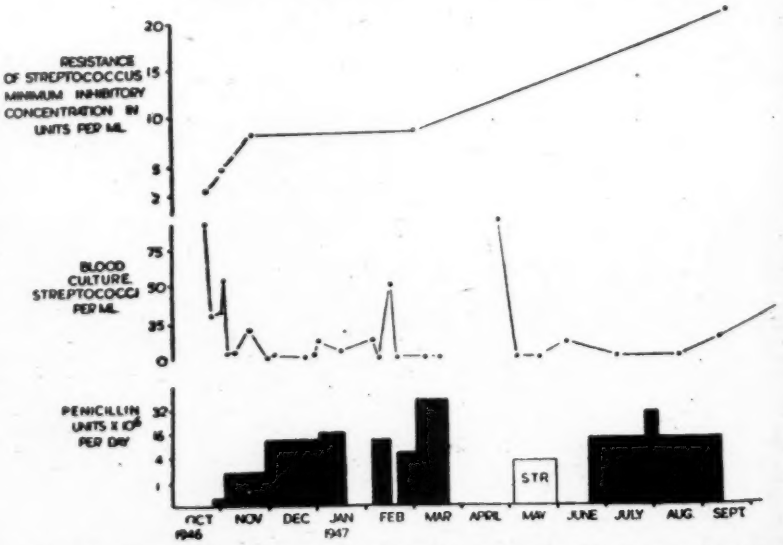

FIG. 1.—Course of events in an ultimately fatal case of subacute bacterial endocarditis due to a streptococcus which underwent a tenfold increase in resistance to penicillin during prolonged treatment with this and other agents. (STR = streptomycin; *p*-aminohippuric acid was also used at some stages in treatment.)

unsuccessful treatment. An example of this was a case of endocarditis lenta described by Dowling *et al.* (1946), in which the streptococcus responsible became progressively more resistant during treatment. We have had a similar experience in this hospital, with the difference that the streptococcus responsible for the endocarditis was originally a resistant one, being inhibited only by 2 units per ml. During prolonged treatment, which included the administration of several thousand pounds worth of penicillin, for one period at the rate of 40 million units daily, as well as other drugs, the degree of resistance of the streptococcus slowly increased: eventually it was inhibited only by 20 units per ml. (Fig. 1).

I have also observed several cases of actinomycosis in which the organism isolated after a period of unsuccessful penicillin treatment was of diminished sensitivity, the difference being about tenfold. In none of these patients is it conceivable that substitution of another organism had occurred, and not habituation of the original one.

Acquired Resistance to Streptomycin

We are faced here with a quite different and indeed unexampled situation, as all species of bacteria can become highly resistant to this drug, often with great rapidity, not only *in vitro* but *in vivo*. Several authors (e.g., Finland *et al.*, 1946; Bondi *et al.*, 1946) have reported the recovery of resistant organisms after only one day's treatment. We have observed this in a *Bacterium aerogenes* urinary-tract infection, the course of which I followed by making quantitative cultures of the urine at frequent intervals (Fig. 2). Only two hours after the first dose of 0.5 g. (repeated four-hourly) the viable count in the urine had fallen from 135,000,000 to only 30,000 per ml.—showing, incidentally, that the action of high concentrations of streptomycin is rapidly bactericidal in the body as well as in the test-tube (Garrod, 1948). The count, repeated at two-hourly intervals during that day, persisted at about the same low level, but after 24 hours had risen again to 5,000,000, and these organisms proved to be 1,000 times more resistant to the drug than those recovered originally. There is evidence (Alexander and Leidy, 1947a) that this remarkable change is due to the existence of a minute proportion of resistant cells in the original population, and it might therefore be possible to predict the result of treatment by cultivating a very large inoculum in drug-containing medium.

I have attempted this in connexion with urinary-tract infections by making pour-plate cultures of the high-speed centrifuged deposit of 10 ml. of urine in agar containing 1,000 μg. of streptomycin per ml. This inoculum is about 1,000 times larger than is usually employed in cultivating urine, and might therefore reveal the presence of a small number of resistant bacteria. These were not detected in any of the following cases in cultures made in the usual way. In 14 cases the heavily inoculated streptomycin plates were sterile, and 12 of these were cured with streptomycin. Treatment was also successful in four patients whose cultures yielded very few colonies (1, 2, 4, and 19). It failed completely in the only two whose streptomycin plates contained numerous colonies, some of which proved also in subculture to be streptomycin-dependent. So far as they go, these findings suggest that the method can be made to yield useful information.

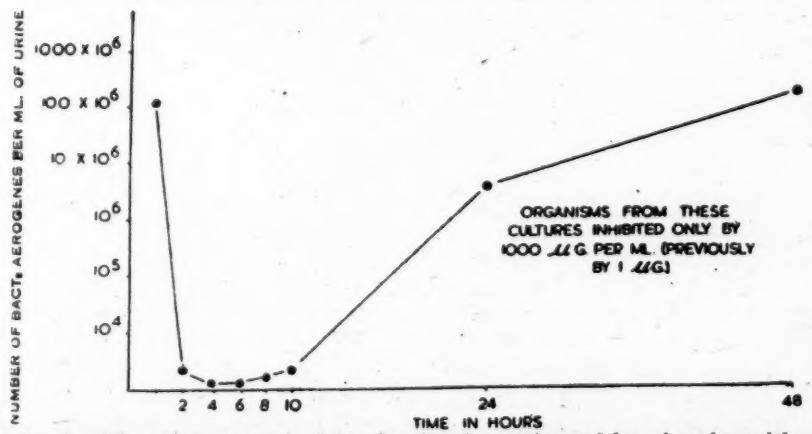

FIG. 2.—Effect of streptomycin (0.5 g. four-hourly, starting at 0 hours) on bacterial content of urine in a case in which treatment failed.

In order to prevent the development of resistance so far as possible, treatment should be vigorous, and for infections other than tuberculosis it need only be so brief that toxic effects have not to be feared. It should also be well timed, particularly in relation to operations, since if it fails there will be no second chance.

Resistance to streptomycin is permanent: hence it needs no great prophetic powers to visualize a time when most of the sensitive bacteria in the civilized world will have acquired it. There are already signs of this: Wilhelm *et al.* (1949) found 85% of strains of *Bact. aerogenes* from urinary-tract infections to be resistant, and in our own experience in this hospital it is becoming common to find resistant strains of this and other coliform bacilli in the urine of patients who give no history of having had the drug. This must mean that they are being disseminated from treated patients. Whether on this account streptomycin should be reserved for treating tuberculosis, as has been seriously suggested, in order to preserve its usefulness for this most important purpose as long as possible, is a matter of opinion. It is of course well known that tubercle bacilli, like other bacteria, can become resistant, although at a slower rate corresponding to their more leisurely growth: this, indeed, is well recognized as the main obstacle to the successful treatment of tuberculosis. Fortunately it appears that the simultaneous administration of *p*-aminosalicylic acid greatly reduces the frequency with which strains of tubercle bacilli become resistant.

Acquired Resistance to Aureomycin and Chloramphenicol

It was originally claimed as one of the advantages of these newer antibiotics that resistance to them does not develop. It is too early to decide how untrue this belief was, but there are signs that the usual process of disillusionment has begun. Certainly, acquired resistance to these drugs is slow to develop, moderate in degree, and not necessarily permanent. Lankford and Lacy (1949), Long *et al.* (1950), and others have found it impossible to habituate staphylococci to "aureomycin" to any serious extent *in vitro*. On the other hand, there are two reports of acquired resistance *in vivo* during treatment, one such case being described by Long *et al.* (1949) and a series by Foley *et al.* (1950). It seems that in some of Foley's cases substitution rather than habituation

may have occurred, but the mere fact that any staphylococcus can possess 64 times the normal resistance is discouraging.

Increases in resistance to aureomycin or chloramphenicol ranging up to about fiftyfold in various species of Gram-negative bacilli have been reported, either produced deliberately or occurring in treated patients. We have seen in this hospital a fifteenfold increase in resistance to chloramphenicol in *Bact. aerogenes* during four days' treatment for urinary-tract infection. How often this kind of thing will occur remains to be seen: so far it seems to be exceptional. Terramycin appears to behave similarly, and it is interesting that organisms made resistant to it also become resistant to both aureomycin and chloramphenicol (Herrell *et al.*, 1950).

Dependence

The strange phenomenon of nutritional dependence on a substance normally lethal is another aspect of the peculiar behaviour of streptomycin. It was first demonstrated in meningococci by Miller and Bohnhoff (1947b), who recognized two types of resistant colonies, one of which proved to consist of organisms that failed to grow at all in the absence of the drug. They behaved in the same way *in vivo*: mice inoculated with them died if treated with streptomycin, but otherwise survived. Soon after this Paine and Finland (1948) showed that dependent mutants could be obtained from various other species. Lenert and Hobby (1949) have also shown that *Mycobacterium tuberculosis* can become dependent.

These cultures are not a mere laboratory freak: they can often be found among resistant organisms in infected urine, and Miller and Bohnhoff (1949) recovered them not only from the pharynx and faeces of treated animals but from the throats of nurses administering the drug. It is theoretically possible that a patient infected with such organisms could be made worse by streptomycin treatment, and improve on its cessation. The patient described by Spendlove *et al.* (1948), from whose sputum dependent tubercle bacilli were isolated 96 days after treatment was begun, is said to have become worse during further treatment and to have remained *in statu quo* since it was stopped.

Further studies of such patients would be of much interest, but in any case it seems highly improbable that converting the organism to dependence and then starving it by withdrawal of the drug will be found a successful method of treatment. Bacterial populations in which such changes are occurring are highly heterogeneous, including organisms possessing varying degrees of simple resistance and some which are still sensitive as well as dependent cells. The observed effects of treatment are a compound of the separate effects on these three types of organism, and their separate assessment seems unlikely to be feasible.

Streptomycin is not the only antibiotic on which organisms can become dependent. Gocke and Finland (1950) have obtained a resistant variant of *Bact. friedländeri* which is strictly dependent for growth on a critical concentration of chloramphenicol. C. P. Miller (personal communication, 1949) has even obtained variants of meningococci which are dependent on penicillin, although only conditionally: they require penicillin for growth in a deficient medium, but grow without it in a richer one.

Stimulation

I propose to deal more fully with the fourth type of bacterial reaction, not because it is more important—although I believe it to be much commoner and more significant than is generally believed—but because it is much less familiar. This is the opposite of the desired effect: the stimulation of bacteria instead of their suppression. There is good evidence that this effect is produced by concentrations lower than those required to inhibit growth: these are naturally very low for sensitive bacteria, but they may be among the highest attainable in the body if the effect is exerted on naturally resistant organisms.

If this is so, it is only an illustration of the Arndt-Schulz law, which, stated shortly, is "Kleine Dosen reizen, grosse Dosen lähmen": in other words, poisons are stimulants in small doses. Schulz (1888) formulated this law as it applies to bacteria over 60 years ago, and since then many workers (Hüne, 1909; Fred, 1911; Hofmann, 1922; Branham, 1929) have shown that low concentrations of a great variety of germicides accelerate bacterial growth. These substances include salts of mercury and other heavy metals, phenols, halogens, arsenical compounds, dyes, and ether. It is an alarming thought that many common disinfectants, if mere traces of them are present, may apparently have precisely the opposite effect to that desired.

Does the Arndt-Schulz law apply to antibacterial chemotherapeutic agents? There is a good deal of evidence that it does. Such as there is with reference to the sulphonamides is unconvincing: Lamanna (1942) used the cup-plate technique, and describes a zone of heavier growth between the zone of inhibition and that of normal growth which he attributes to stimulation In interpreting this and many other observations made by this method it must be remembered that colonies at the boundary of the inhibition zone can obtain an extra supply of nutriment from this unoccupied area, which may sometimes be the whole explanation of their greater size. There has been little suggestion from the clinical side that sulphonamides can behave in this way, but in one of the U.S. Naval training centres in which sulphadiazine prophylaxis led to the prevalence of resistant haemolytic streptococci, scarlet fever and other infections became more common in treated than untreated men. The authors of the report on this epidemic (Epidemiology Unit 22, 1945) discuss the possibility that the drug was acting as a growth stimulant to these resistant streptococci.

If penicillin can stimulate bacterial growth it is perhaps a more serious matter, and there is a good deal of evidence that it can. From the clinical point of view this evidence rests largely on the occurrence of what have been called "superinfections" during penicillin treatment. It is well known that during local treatment of the mouth and throat the normal flora is largely replaced by resistant coliform bacilli (Long, 1947). The same thing can happen elsewhere with more serious results: Weinstein (1947) and Appelbaum and Leff (1948) report cases in which resistant Gram-negative organisms appeared as the cause of pneumonia during penicillin treatment for an originally sensitive infection The full account given by Stanley (1947) of 10 cases of *Pseudomonas pyocyanea* infection is interesting: he does not seem to suspect that penicillin had anything to do with producing or aggravating these infections, but in fact seven of his patients, six of whom died, were treated with penicillin either shortly before or during the progress of the infection.

How is this substitution of resistant for sensitive organisms to be explained? Some authors apparently

take the view that the elimination of existing bacteria leaves a kind of vacuum which is bound to be filled by others. This view seems justified only if we assume that the normal balance is maintained by antibiosis. It is certainly not the explanation of all cases, because during penicillin treatment resistant bacteria may appear where no bacteria at all were before. This seems particularly apt to happen in the urinary tract during the excretion of penicillin given for disease elsewhere. Three of our patients under treatment for bacterial endocarditis have developed urinary infections due to *Ps. pyocyanea* for no apparent reason other than the presence of the drug in the urine. We have also seen a rapidly fatal pyaemia due to this organism develop during the treatment of a case of actinomycosis, the portal of entry being the vein into which the drug was being given by continuous drip (Christie and Garrod, 1944).

If penicillin does stimulate or accelerate bacterial growth it should be possible to demonstrate this *in vitro*. This has in fact been done by several different methods. Pratt and Dufrenoy (1947) and Van Marwyck (1949) used the agar diffusion technique, obtaining a zone of enhanced growth external to that of inhibition: that caution is required in interpreting this appearance has already been pointed out, but the results of Eriksen (1945), who obtained a zone of enhanced growth with no inhibition zone internal to it, suggest that such appearances may be due to true stimulation. Curran and Evans (1947) found that the germination of spores and the growth of staphylococci and streptococci in a skim-milk medium were accelerated by low concentrations of both penicillin and streptomycin. Miller *et al.* (1945) cultivated *Staphylococcus aureus* in broth containing different concentrations of penicillin, estimating the amount of growth turbidimetrically: sub-inhibitory concentrations enhanced it, and it is interesting that maximum enhancement was produced by an amount of penicillin only about one-fifth of that required to inhibit growth completely. The difference between the stimulating and inhibiting concentrations of ordinary germicides is far wider than this. There are also two recorded examples of experimental *in vivo* stimulation: Randall *et al.* (1947) found that subcurative doses of penicillin increased the mortality from *Salmonella typhi* infection in mice, and Foley and Winter (1949) showed that penicillin increases the mortality of chick embryos inoculated with *Candida albicans*.

I have made some observations recently on the acceleration of bacterial growth by penicillin, using the method of Aoki *et al.* (1949), which is simply a comparison of the size of colonies on penicillin-containing and normal media. There is no doubt that such acceleration occurs: it is caused by appropriate concentrations in both sensitive and resistant species, such as 0.004 unit per ml. for a staphylococcus (Fig. 3) and 4 units or more for *Ps. pyocyanea* (Fig. 4). But the differences in colony size are variable, and some of the factors responsible for this remain to be worked out. One is certainly the age of the culture used for inoculating the plates: it seems that penicillin particularly stimulates the growth of relatively dormant cells from older cultures. Another is the medium: the poorer this is, the greater the effect. The greatest contrast in colony size I have seen was in *Ps. pyocyanea* growing on a medium consisting simply of urine solidified with agar. A third appears to be temperature, the contrast being more marked in cultures maintained a few degrees below 37° C. It is interesting that stimulation should be enhanced by three factors in themselves unfavourable to growth: two of these seem to afford a clue to the mechanism whereby previously dormant bacteria may become active in the body.

I have hitherto deliberately avoided any mention of the tubercle bacillus in this connexion. Like *Ps. pyocyanea* it is highly resistant to penicillin, and forms penicillinase: does it react to the drug in the same way? It is some years since Ungar and Muggleton (1946) claimed to have shown that penicillin stimulates the growth of *Myco. tuberculosis* in a liquid medium: Iland and Baines (1949) could not confirm this result, but they used higher concentrations of penicillin, and their

FIG 3.—Divided agar plate culture of *Staph. aureus* (Oxford "H" strain, of normal penicillin sensitivity). Medium in the right half contains 0.004 unit of penicillin per ml. Incubated at 35° C. for 17 hours.

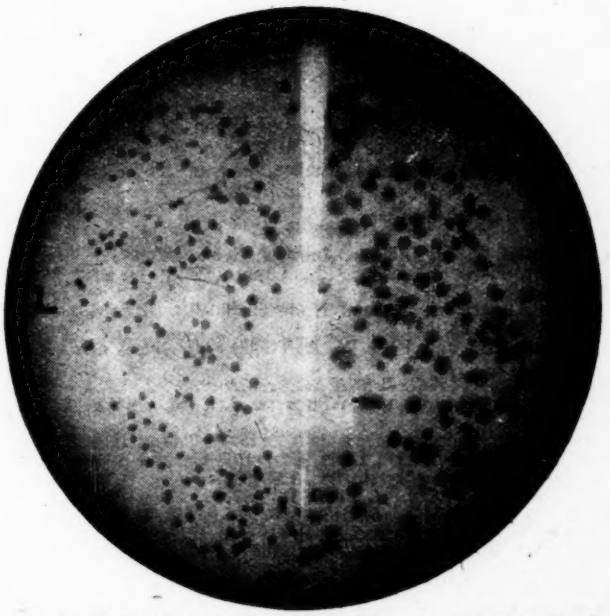

FIG. 4.—Divided agar plate culture of *Ps. pyocyanea* inoculated from a broth culture 1 week old, and incubated at 37° C. for 17 hours. Medium in the right half contains 4 units of penicillin per ml. Not only are the colonies larger on this side, but pigment formation was much more pronounced.

criticism of Ungar and Muggleton's work ignores some of the controls used by these workers. Rivière *et al.* (1947) also reported that penicillin greatly accelerates death from tuberculosis in guinea-pigs, but penicillin is so exceptionally toxic to this animal that uninoculated but treated controls have shown an unduly high mortality in the hands of other workers, and Rivière's conclusion is not accepted. My colleague, J. W. S. Blacklock, and I have been much interested in this problem, and he has recently carried out similar experiments in mice, but without being able to show that penicillin aggravated the disease.

Evidence from the laboratory is therefore inconclusive and I hesitate, as a mere laboratory worker, to import clinical evidence into this argument. Nevertheless one cannot but be impressed when a patient under treatment with penicillin for a staphylococcal lung abscess is found to have tubercle bacilli in his sputum, none having been present before, and dies of acute tuberculosis one month after the starting of treatment. I have certainly formed the impression from the examination of specimens and from post-mortem findings in a number of cases that during treatment with penicillin for some other condition a previously unrecognized or relatively quiescent tuberculous focus may become active: either bacilli appear where none were found before, or their numbers increase enormously. This is only an impression, and it may be false: I can therefore go no further than to suggest that if penicillin is used in a patient who incidentally has tuberculosis the possible effects on that disease are worth watching.

Conclusion

I hope I have said enough to convince you that bacteria are displaying some versatility in their response to chemotherapeutic drugs. They are not taking the present widespread attack on them lying down: some are defending themselves very effectively, and some are even turning our weapons to their own advantage. So far the supply of new antibiotics has more than matched the capacity of bacteria to resist them, but if this supply should cease—and presumably the number yet to be discovered is limited—the time may come when a few of the more enterprising species will flourish more or less unhindered.

I am indebted to my clinical colleagues at St. Bartholomew's Hospital for permission to mention their cases, to Miss P. M. Waterworth for technical assistance, and to the photographic department of the hospital for illustrations.

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The Chemical–Biological Co-ordination Centre of the National Research Council of the United States has announced the publication of the third volume in its series of reviews concerned with chemical-structure-biological-activity relationships. *Histamine Antagonists* (122 pp., $1.50), by Drs. Frederick Leonard and Charles P. Huttrer, discusses the pharmacological properties, methods of *in vitro* and *in vivo* evaluation, methods of synthesis, structure-activity relationships, mechanism of action, and clinical application of histamine antagonists. More than 1,000 compounds which have been tested for potential antihistaminic activity are listed in 48 classified tables including structures, activities, and literature references. Emphasis is placed on the analysis of structure-activity correlations within the different classes of compounds and on generalizations which can be deduced. The review contains 224 references.

DIAGNOSIS OF AORTIC STENOSIS

BASED ON A STUDY OF 25 PROVED CASES

BY

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Aortic stenosis is an important clinical entity which often escapes recognition in life. Reliance upon gross physical signs of the valvular lesion will allow diagnosis of only one-quarter of the cases to be found at necropsy (Parkinson, 1949). Routine necropsies also show that in one-half of the cases in which stenosis is present there is no other valvular lesion, and that most patients with *lone* aortic stenosis eventually die from heart failure or infective endocarditis as a result of their valvular disease.

This paper, based on a study of 25 proved cases, shows that aortic stenosis is common, and that a correct clinical diagnosis should be possible in a high proportion of cases. It is also submitted that lack of familiarity with the natural history of aortic stenosis as well as the demand for too rigid diagnostic criteria is chiefly responsible for the common failure to diagnose the condition.

Material

Amongst 2,245 routine necropsies performed at the Postgraduate Medical School of London during the seven-year period ending in February, 1950, aortic stenosis was found in 45 cases (1.8%). Of these 45 cases calcareous aortic stenosis was the only significant valvular lesion in 25; in the remaining 20 all degrees of aortic stenosis were found—16 were complicated by mitral stenosis, three by gross aortic incompetence, and one by tricuspid stenosis and mitral stenosis.

As it was thought that the clinical problem of aortic stenosis could be studied satisfactorily only when uncomplicated by other valvular lesions, detailed analysis has been confined to the first group of 25 cases (Table IV, overleaf). The degree of stenosis at necropsy was graded as mild, moderate, or severe, depending upon whether the aortic orifice would admit the index finger, a finger-tip, or less than a finger-tip respectively (Kumpe and Bean, 1948).

Of these 25 cases significant aortic stenosis was a coincidental necropsy finding in three in which death was due to non-cardiac causes. Twenty-two patients first came under medical observation on account of cardiac or cerebral symptoms; 15 died from heart failure consequent upon the valvular lesion and four from infective endocarditis (Table I).

TABLE I.—*Cause of Death in 25 Cases of Aortic Stenosis*

	No. of Cases
Heart failure from aortic stenosis	15
Heart failure from aortic stenosis and myocardial infarction	2
Bacterial endocarditis	4
Heart failure	3
Cerebral embolism	1
Rupture of dissecting aortic aneurysm	1
Bronchopneumonia	2
Cerebral metastasis from bronchial carcinoma	1

Clinical History

The majority of patients had spent a long life of activity and usefulness untroubled by heart complaints until the sixth or seventh decade. The onset of symptoms was commonly sudden (Tables II and III), and was attended by a serious prognosis.

The total duration of cardiac symptoms was less than four years in four-fifths of the cases. Valvular disease had been diagnosed 16 to 30 years before symptoms appeared in four patients; all lived active lives in the interim, and two were professional footballers. The extent of calcification of the aortic valves at necropsy indicated that significant stenosis had been of long standing in every case in the series. There was thus good reason to believe that most of them had enjoyed long periods of good health in the presence of unsuspected valvular disease.

TABLE II.—*Presenting Symptoms in 22 Cases of Aortic Stenosis*

Symptom	No. of Cases
Exertional dyspnoea	11
Nocturnal dyspnoea	3
Cardiac pain	3
Syncope	2
Giddiness	2
Stroke	1

TABLE III.—*Frequency of Symptoms in 22 Cases of Aortic Stenosis*

	No. of Cases
Exertional dyspnoea	19
Nocturnal dyspnoea	10
Cardiac pain	10
Palpitation	4
Attacks of pallor and sweating	4
Cerebral symptoms:	
Giddiness	8
Syncope	4
Mental confusion	4
Fits	2
Maniacal violence	2
Stroke	1

Characteristic clinical histories demonstrate how the patients first came under medical observation, as well as the course of the terminal illness.

Case 1: Lassitude and Giddiness

A 70-year-old baker had had valvular disease diagnosed 16 years previously. In spite of this he had enjoyed good health until three months before admission, when he complained of gradual failure of vision and increasing lassitude. Two months later postural giddiness set in. Ten days before admission he experienced a sensation of "water streaming down in the air" past his head. This symptom never left him and kept him awake at night. On admission there were classical signs of aortic stenosis (Table IV). Heart failure was absent and the electrocardiogram showed sinus rhythm and left bundle-branch block. His symptoms improved in hospital, but persisted until the final admission a year later. Ten days previously, while taking a meal, a small piece of bread stuck in his throat, and he gasped for breath. Severe breathlessness persisted from this moment. Unable to lie flat, he remained in a chair until admission.

On examination there was severe congestive heart failure. The pulse rate was 32 a minute, and the electrocardiogram confirmed complete heart-block. The aortic systolic thrill previously felt could not be detected terminally. Heart failure showed little response to treatment, and he became mentally confused, with lucid intervals during the day. Death took place suddenly while drinking a cup of tea, two weeks after admission and 15 months after the first symptom.

Post-mortem examination revealed acute pulmonary oedema and severe aortic stenosis with gross calcification of the cusps. Calcium deposits encroached upon the interventricular septum, and microscopically there was myocardial fibrosis underlying the calcification in the neighbourhood of the bundle of His.

Case 4: Cardiac Pain and Giddiness

A 63-year-old foreman had been well until six months previously, when he noticed pain in the throat and upper chest, brought on by exercise and relieved by rest. Giddiness on exertion was also troublesome. On the day of admission, while walking in the street, he bent down to do up a shoelace, and suddenly became extremely short of breath. Struggling to his doctor, he began coughing up blood-stained sputum. On admission a diagnosis of hyper-

TABLE IV.—*Clinical and Post-mortem Findings in 25 Cases of Calcareous Aortic Stenosis*

Case	Sex	Age	No. of Admissions	History of Rheumatism	Total Length of History	Pulse: Rate/min.	Pulse: Rhythm	Pulse: Volume	Apex Beat Displaced	Thrill	Systolic Murmur: Aortic	Systolic Murmur: Mitral	Diastolic Murmur	Aortic 2nd Sound	Triple Rhythm	Blood Pressure	Degree of P.M. Stenosis	Weight of Heart (g.)	Clinical Diagnosis
1	M	70	2	+	15 mths	32	Reg.	Small	+	Aortic	++	+	++	Absent		170/60	Severe	690	Aortic stenosis. Complete heart-block
2	M	63	2	+	5 ,,	100	,,	Collapsing	+	,,	+	+	+	(I & II) (distant)		120/60	Mod.	540	Infective endocarditis Aortic valve
3	M	65	—	—	5 yrs	100	,,	Normal	+		+	+	+	Normal		150/110	Mild	490	Chronic bronchitis. Emphysema. Heart failure
4	M	63	2	—	9 mths	88	,,	,,	+		+	+	+	—		105/75	Severe	750	Calcareous aortic stenosis
5	F	72	—	—	1 yr.	130	Aur. fib.	Small	+	Aortic	+	+	+	—		130/85	Mod.	780	Thyrotoxic heart failure
6	M	57	1	—	3 mths	138	,,	Bounding	+		+	+	+	—		134/105	Severe	450	Aneurysm of aorta. Aortic stenosis
7	M	65	1	—	2 wks	60	Reg.	Small	+		+	+	+	(I & II) (distant)		105/75	Mod.	—	Coronary thrombosis
8	M	53	—	—	—	80	,,	Normal	No		+	+	+	—		120/80	Mild	300	Carcinoma of stomach
9	M	78	—	—	—	88	,,	Full	No		+	+	+	—		115/75	,,	300	Aortic incompetence. Bronchopneumonia
10	M	49	2	—	4 yrs	82	,,	Anacrotic	+	Aortic and mitral	+	+	+	(I & II) (distant)		120/80	Mod.	730	Aortic stenosis. Heart failure
11	M	77	1	—	10 days	160	Aur. fib.	—	—	—	Nil	Nil	Nil	Dim.		108/85	Mild	350	Hypertensive heart disease
12	M	71	1	—	7 wks	80	Reg.	Normal	+	Aortic	+	+	+	—		130/85	Mod.	450	Aortic stenosis. Anaemia
13	M	43	1	+	5 ,,	102	,,	Collapsing	+	Aortic and mitral	+	+	+	—		140/70	,,	660	Aortic stenosis and incompetence. Bacterial endocarditis
14	M	61	2	+	6 mths	132	,,	Dicrotic	+	Aortic	+	+	+	Absent		110/90	Severe	765	Aortic stenosis. Heart failure
15	F	75	1	+	3 ,,	100	Aur. fib.	—	+	—	+	+	+	—		120/65	Mod.	740	Rheumatic heart disease. Heart failure
16	F	78	2	+	1 mth	84	,,	Dicrotic	+	Mitral	+	+	+	Absent		120/70	Mild	560	Aortic stenosis. Bacterial endocarditis
17	M	72	2	+	14 wks	80	Reg.	—	+	—	Nil	Nil	Nil	(I & II) (distant)		170/100	Mild	535	Hypertensive heart failure
18	M	52	3	+	12 mths	84	,,	—	+	Aortic	+	+	+	Loud		110/60	Mod.	1,020	Aortic stenosis and incompetence. Mitral stenosis
19	M	64	1	—	6 wks	80	,,	Small	+	,,	+	+	+	(I & II) (distant)	+	120/60	,,	565	Aortic stenosis. Syphilitic aortitis
20	F	74	2	—	7 ,,	84	,,	Anacrotic	+	—	+	+	+	Dim.	+	170/140	,,	575	Hypertensive heart failure
21	F	56	2	—	2 yrs	112	,,	Full	+	Mitral only	+	+	+	Absent	+	100/85	Severe	—	Calcareous aortic stenosis. Heart failure
22	F	78	2	—	9 mths	118	,,	,,	No	—	+	+	+	Normal	+	115/75	Mild	360	Aortic stenosis. Heart failure
23	M	68	—	—	—	80	,,	—	+	—	+	+	+	—	+	180/80	,,	—	Carcinoma of bronchus. Aortic stenosis
24	M	76	1	—	4 yrs	75	,,	Normal	No	—	+	+	+	(I & II) (distant)	+	140/85	Mod.	574	Coronary artery disease. Heart failure
25	M	62	3	—	4 ,,	85	,,	Small	—	—	+	+	+	Normal	+	130/80	,,	470	Carcinoma of bronchus
Totals or averages	M 19 F 6	63·6 72·2	1·8	4	14 mths	94	Aur. fib. 5	Small 9 Full 5	16	Aortic 9 Mitral 4	21	21	12	Absent 4 Dim. 2 Normal 3	4	130/80	Mild 7 Mod. 13 Severe 5	389 597 664	Aortic stenosis 13

+ = Present. — = Not recorded. P.M. = Post-mortem examination. >, =, or < = Greater than, equal to, or less than, respectively. Aur. fib. = Auricular fibrillation.

tensive left ventricular failure was made. Response to treatment was satisfactory, and he was discharged within a month. On readmission two months later, little history could be obtained on account of the patient's confused mental state. He told of four weeks' nocturnal breathlessness and severe exertional chest pain, radiating down the left arm.

On examination there was little evidence of heart failure, but respiration was of the Cheyne–Stokes type. Aortic stenosis was diagnosed on the basis of a rough aortic systolic murmur (Table IV). The patient subsequently became violent, abusive, and mentally confused, though he had remarkably lucid intervals, and died six days after admission, nine months after his initial symptoms. The mode of death was curious: there was no complaint of breathlessness or any true orthopnoea. There was no peripheral oedema, and the jugular venous pressure was not raised. Mental confusion was the sole manifestation of failure; yet the patient was able to recognize his own Cheyne–Stokes respiration by remarking that he breathed "too much in fits and starts."

Post-mortem examination showed severe aortic stenosis and acute pulmonary oedema.

Case 12: Syncopal Attacks

A healthy old-age pensioner of 71 years, while sitting in a public-house, fell unconscious without warning. There was no fit; recovery of consciousness was rapid, and he soon felt well enough to go home. One week later, while sitting in front of the fire, he had another similar fainting attack. He recovered consciousness after two minutes and passed the incident off as "a joke." Subsequently he felt well and was admitted for investigation of the syncopal attacks, which were his only complaint. A clinical diagnosis of aortic stenosis and anaemia without heart failure was made (Table IV). Nine days after admission and seven weeks after the first syncopal attack he became mentally confused, with temporary cyanosis followed by pallor, urgent dyspnoea, and moist sounds throughout both lung fields. Heart failure, which proved to be terminal, showed no response to treatment, and death took place from left ventricular heart failure 30 hours later.

Post-mortem examination confirmed the clinical findings, showing a moderate degree of aortic stenosis.

Case 13: Infective Endocarditis

A 43-year-old accountant was admitted to hospital on account of weakness and chest pain. Valvular heart disease had been diagnosed at the age of 10 years, following rheumatic fever. Subsequently he had enjoyed good health apart from recurrent winter bronchitis until one month before admission. After removal of septic teeth at this time he noticed increasing lassitude and breathlessness on exertion. Two weeks later sharp back pain, which lasted a week, was followed by persistent "gnawing" pain in the chest, radiating down the inner and outer aspects of the left arm.

On admission continuous chest pain was his chief complaint. A clinical diagnosis of bacterial endocarditis developing upon aortic valve disease was made (Table IV). Heart

failure was absent at first, but the electrocardiogram showed changes consistent with posterior cardiac infarction. The infection was treated with sulphonamides without response, and rapidly progressive and unresponsive heart failure supervened. Ten days after admission and five weeks after the first symptom there was sudden collapse, with pallor, sweating, and intense dyspnoea, and death took place in six hours.

Post-mortem examination confirmed pulmonary oedema as the cause of death. Friable vegetations were confined to a moderately stenosed and incompetent aortic valve, but a mycotic aneurysm was found arising from the anterior sinus of Valsalva. This had compressed the left coronary artery, with consequent recent anterior myocardial infarction.

Case 19: Left Ventricular Heart Failure

A previously healthy 64-year-old bricklayer developed a nocturnal cough which was relieved by sitting up in bed. He also noticed exertional dyspnoea during the day: "If I walked 100 yards it felt as though I had run the same distance." His nights became progressively more disturbed by cough, breathlessness, and, latterly, by upper-abdominal pain. He was admitted to hospital after an attack of severe abdominal pain and breathlessness during the early hours of the morning. Congestive heart failure was not evident at this time, and the signs in the chest were regarded as due to pneumonia, although the chest film suggested pulmonary oedema. Aortic stenosis was recognized clinically (Table IV); but treatment was unsuccessfully directed towards bronchopneumonia, which was strongly suggested on clinical grounds. Five days after admission and six weeks after the first symptom of illness the patient died suddenly from acute pulmonary oedema while using a bedpan.

Post-mortem examination showed moderate aortic stenosis, acute pulmonary oedema, and large bilateral pleural effusions, but no evidence of pulmonary infection.

Physical Signs

Pulse.—The rhythm was regular except in five cases with auricular fibrillation. Of the 20 cases in which the volume was recorded a small pulse was noted in less than half; an anacrotic pulse in five cases was always good evidence of moderate or severe stenosis, but in an equal number, including two cases with advanced stenosis, the pulse was full or collapsing. In one-third of the cases correctly diagnosed in life the pulse was recorded as normal or full.

Apex Beat.—The cardiac impulse was displaced to the left in two-thirds of the cases; in five it was heaving, and was twice noted to be of a slowly rising character. In one-fifth of the series the apex beat was in a normal position.

Aortic Systolic Thrill.—A systolic thrill felt in the second right intercostal space in one-third of the cases invariably indicated moderate or severe stenosis. A systolic thrill was confined to the mitral area in one case with a slit-like valvular opening, 4 by 1 mm. In a similar case, in which the aortic orifice was described as of "pinhole" size, a basal systolic thrill was hardly palpable. Two cases with moderate stenosis had thrills equally intense at apex and base, and in a third case it was felt only in the third left intercostal space. A correct clinical diagnosis was made in five cases without a basal systolic thrill.

Aortic Systolic Murmurs.—A loud harsh aortic systolic murmur conducted to the neck was heard in four-fifths of the cases. In an equal proportion a harsh mitral systolic murmur was recorded. In six cases, of which five had advanced stenosis, the mitral murmur was loud and rough, exceeding in intensity the signs at the base. Widespread systolic murmurs were noted in one-fifth of the series; in two cases no murmurs were heard at any time throughout the illness although they were repeatedly sought. A correct clinical diagnosis was made in three cases in which a harsh aortic systolic murmur was the only physical sign of the valvular lesion.

Aortic Diastolic Murmurs.—These were recorded in just under half of the series, and were most obvious when bacterial endocarditis involved the aortic cusps. Diastolic murmurs, sometimes noted as harsh, but usually short and soft, were heard in both the cases of extreme stenosis.

Aortic Second Sound.—The aortic second sound was absent in four patients, in three of whom stenosis was severe; in two with moderate stenosis it was diminished; and in three, including one with gross stenosis, it was normal. Frequently both heart sounds were equally diminished, but in one case of moderate stenosis the aortic second sound was accentuated.

Blood Pressure.—Blood-pressure readings did not conform to the expectation that both systolic and pulse pressures should be low (Christian, 1931). The average reading for the series was 130/80 mm. Hg. Four cases with a pulse pressure less than 30 mm. Hg had severe stenosis. Otherwise blood-pressure readings were of little value in diagnosis. Wide pulse pressures in the absence of significant aortic incompetence were noted, the highest figure of 110 mm. Hg (Case 1) being recorded in the presence of extreme stenosis. Diastolic blood pressures of 100 mm. Hg or more were found in four cases. It was important to distinguish, retrospectively, between benign hypertension and hypertension contingent upon left ventricular failure in this series. This may not always be possible when a case of aortic stenosis is seen for the first time in acute heart failure. Normal systolic and diastolic pressures greatly increased when terminal heart failure supervened in two patients, and in another the sudden onset of left ventricular failure raised the blood pressure from 170/140 to 250/160 mm. Hg (confirmed by repeated observations).

Triple Heart Rhythm.—This was heard in six cases; in four it persisted throughout the final illness and in two it was transient.

Electrocardiography

Limb lead tracings, and usually chest leads, were recorded in 20 cases. In no case was a normal tracing seen (Table V). Left ventricular preponderance was common, but its detection was not always possible from the standard leads alone, especially in the presence of bundle-branch block. Myocardial infarction with necropsy control was diagnosed once. A cardiographic diagnosis of pericarditis was later confirmed at necropsy in one case to be due to intrapericardial haemorrhage from a ruptured aorta. Only once was aortic stenosis diagnosed on the basis of characteristic S-T changes, but the clinical signs of the lesion were obvious.

TABLE V.—*Electrocardiographic Findings in 20 Cases of Aortic Stenosis*

	No. of Cases
Left ventricular preponderance:	
Slight	4
Moderate	6
Severe	3
Auricular fibrillation	4
Prolonged P-R interval	4
Bundle-branch block (left 5, right 1)	6
Complete heart-block	1

Radiography

Every patient was submitted to radiological study. This was often confined to portable chest films, as many were too ill for more detailed investigation. Cardiac enlargement was reported in 21 cases and isolated or disproportionate left ventricular enlargement in 18 of these. Pulmonary congestion or pleural effusion was a usual accompaniment of cardiac enlargement. Aortic unfolding was the rule and frequently this was advanced. Associated heart failure and unfolding of the aorta obscured the classical radiological appearances of aortic stenosis in every case.

Gross aneurysmal dilatation of the ascending aorta was observed in two patients. In Case 6, at post-mortem examination, a syphilitic aneurysm was found to be associated with extreme aortic stenosis. Histological examination failed to demonstrate either a syphilitic or rheumatic basis for the stenosis. In Case 7 a dissecting aneurysm of the aorta, which finally ruptured into the pericardial sac, was associated with moderate aortic stenosis. Microscopical examination revealed medial necrosis of the aorta.

Calcification of the aortic valves, demonstrated in three of the five cases in which it was specifically sought and observed only by fluoroscopy, permitted a certain clinical diagnosis of aortic stenosis in one case in which the only other physical sign of the lesion was an aortic systolic murmur.

Clinical Course

A rapidly downhill course with death from heart failure was the rule, and was seen in 22 cases. In this group the average survival was 14 months from the first symptom of illness. In the final phase heart failure was peculiarly resistant to treatment, and death took place within three weeks of hospital admission in more than two-thirds of the cases. Nearly half the patients died on the first admission, and only two survived a second stay in hospital.

Sweating attacks associated with striking pallor were seen in four cases during the terminal stages of heart failure. Mental confusion, epileptiform convulsions, or maniacal violence was a terminal event in seven cases. Seven patients, all of whom were in heart failure, died suddenly or unexpectedly within seconds or minutes. Three of these gave a clear history of anginal pain; acute pulmonary oedema was confirmed at necropsy in five, and in one there was recent myocardial infarction.

Frequency of Correct Clinical Diagnosis.—Aortic stenosis was recognized in life in 13 of the 25 cases. The frequency of correct diagnosis was related to the degree of stenosis found at necropsy (Table IV). Clinical diagnosis was always correct when stenosis was severe; 6 of the 13 moderately severe cases were diagnosed in life, while five of the seven mild cases escaped clinical detection.

Discussion

Incidence of Aortic Stenosis

This study confirms the frequent observation that the maximum incidence of symptoms due to an isolated aortic stenosis is in the sixth and seventh decades and that males are affected about three times as often as females (Table IV). The incidence of all cases of aortic stenosis (with and without other valvular lesions) in the present series agrees precisely with the findings of McGinn and White (1934) in 6,800 routine necropsies (1.8%). Amongst 630 patients dying from rheumatic valvular disease, Clawson *et al.* (1938) found that calcified nodular deformity of the aortic valve constituted 41% of valvular deformities and 31.5% of all rheumatic heart disease. Finally, Kumpe and Bean (1948) identified *isolated* calcareous aortic stenosis in 0.72% of 15,016 necropsies, comparable to the present findings of nearly 1%.

Compared with congenital heart disease aortic stenosis is common. Gelfman and Levine (1942), analysing 34,023 necropsies, discovered significant congenital cardiac defects after the age of 2 years in 0.53% of cases. These figures suggest that after infancy aortic stenosis, both isolated and combined with other valve lesions, is more than three times as common as congenital heart disease.

Clinical Features

Karsner and Koletsky (1947) have put forward convincing pathological evidence that the aetiology of aortic stenosis is nearly always rheumatic. A past history of rheumatism, however, contributes even less to the diagnosis of aortic stenosis than it does in mitral valvular disease. This is indicated by a rheumatic history in less than one-sixth of the present series, and by the extreme variations in the incidence of past rheumatism in other published figures: 66% (Kumpe and Bean, 1948); *nil* (Kiloh, 1950).

The degree of necropsy calcification which has developed upon a still older scarring process in the aortic valve suggests a very prolonged and slow development. This is borne out by the not infrequent recognition of aortic stenosis in early middle life—a symptomless course, lasting for decades, with frequent termination after the age of 60. When symptoms finally develop the earliest complaints are commonly exertional or nocturnal dyspnoea, cardiac pain, giddiness, or syncope. Mental disorder may appear early (Kumpe and Bean, 1948). Breathlessness, whether exertional or paroxysmal, is often precipitated by unaccustomed exertion or emotion, and tends to progress rapidly. Cardiac pain, which is common, may be independent of any associated hypertension, aortic incompetence, or coronary vascular disease (Contratto and Levine, 1937). The present study confirms the observation of Kumpe and Bean (1948) that cardiac pain is an index of advanced stenosis and suggests that patients afflicted by it are liable to sudden death.

Attacks of giddiness or syncope assume special diagnostic importance when they follow some unaccustomed exertion. Syncope, however, may occur at rest and, rarely, may be precipitated by the development of complete heart-block complicating the valvular lesion. Stokes-Adams attacks may occur (Contratto and Levine, 1937). Sudden death, so common during the final illness in this series, may be the only clinical manifestation of aortic stenosis (Marvin and Sullivan, 1935; Dry and Willius, 1939).

The high incidence of infective endocarditis in this series (4 cases out of 25) agrees closely with the findings of Contratto and Levine (1937). Early diagnosis of symptomless aortic stenosis is therefore of the utmost importance in that steps may be taken to reduce the very real risk of infective endocarditis to which these patients are liable.

On the basis of the classical signs of (1) a slowly rising pulse, (2) an aortic systolic murmur and thrill, and (3) an absent aortic second sound, only one-sixth of the present cases would have been recognized clinically. This fits in with the statement by Wiggers (1944), that so long

as compensation persists the aortic orifice must be reduced to less than one-quarter of its natural size before systolic discharge, blood pressure, or pulse form is affected.

Lewis (1940) taught that a slowly rising pulse was an essential accompaniment of any significant degree of aortic stenosis. The findings in this series and the observations of McGinn and White (1934) are opposed to the general truth of this teaching. Even allowing for the fact that the art of detecting minor changes in pulse volume at the bedside is fast being lost, the present study has shown that advanced aortic stenosis may be accompanied by a full or even a collapsing pulse.

A systolic thrill in the second right intercostal space was the most reliable sign of aortic stenosis in this series. It is well known that in the presence of heart failure the systolic thrill of aortic stenosis may become less intense or even disappear. In lesser degrees of aortic stenosis, and especially in the presence of heart failure, a thrill may be detected only by placing the outstretched hand firmly against the praecordium during expiration with the patient sitting well forward.

The finding of a thrill at or near the mitral area in nearly one-sixth of the reported cases emphasizes a variant in aortic stenosis which is often misinterpreted at the bedside and is rarely mentioned in clinical teaching.

A thrill felt in the neck should be accepted as evidence of aortic stenosis only when it is long and is accompanied by a rough systolic murmur in the aortic area. A short thrill in the root of the neck may occur in health, especially in young people. In the presence of significant incompetence the systolic thrill of aortic stenosis may reveal itself by a carotid shudder visible in the neck. When this sign is present it is by itself reliable evidence of the dual lesion (Evans and Lewes, 1945).

A loud harsh systolic murmur in the second right intercostal space, conducted into the neck, was the commonest clinical sign of aortic stenosis. It was a careful appraisal of this murmur that led to a correct clinical diagnosis in four cases without a systolic thrill. It is important to emphasize how often the systolic murmur of aortic stenosis is audible over a wide area and how commonly the murmur is loudest in the mitral area, to which it may occasionally be confined. The recognition of this fact should help to guard against the unwarranted diagnosis of mitral incompetence in such cases.

Aortic diastolic murmurs may be anticipated in about half the cases of aortic stenosis. The discovery of a harsh aortic diastolic murmur in cases of valvular disease should suggest the possibility of aortic stenosis as well as of incompetence.

The appraisal of a harsh basal systolic murmur in the absence of any of the expected signs of aortic stenosis may offer a difficult diagnostic problem. The teaching of Sir Thomas Lewis (1940), however, that it is unpardonable to diagnose aortic stenosis on the basis of an aortic systolic murmur is not generally accepted (McGinn and White, 1934; Contratto and Levine, 1937; Willius, 1939; White, 1944; Evans, 1948). The statement of White (1944) that the diagnosis can be made on the aortic systolic murmur alone in a patient without aortic dilatation or hypertension, provided the murmur is loud and harsh, is supported by this study. There is abundant evidence that aortic stenosis may declare itself by an aortic systolic murmur as the only physical sign; for both Willius (1939) and Baker *et al.* (1943) emphasize that patients seen one or two decades before death from aortic stenosis had basal systolic murmurs, often without symptoms and sometimes dismissed as innocent or functional. All cases of suspected heart disease, therefore, with rough systolic murmurs, especially at the aortic area, should be carefully examined with aortic stenosis in mind, and submitted to fluoroscopy for the detection of calcification of the aortic valve.

An absent second sound in the aortic area is good evidence of advanced stenosis but it was not a common finding in this study. Evaluation of a diminished second sound at this site is often difficult, especially in the presence of heart failure, when the pulmonary second sound may be accentuated. Since a normal and even accentuated second sound may accompany established stenosis, failure to detect any audible abnormality other than a systolic murmur should not weigh too heavily against the diagnosis.

The unreliability of blood-pressure readings as a diagnostic guide in the study is also emphasized by the finding by McGinn and White (1934) of "an unexpectedly high figure" of 60 mm. Hg for the mean pulse pressure in their series and by the observation of Kumpe and Bean (1948) that in their cases blood-pressure readings were so different from the classical description that sometimes they actually biased the observer against the correct diagnosis.

Triple rhythm, rarely mentioned in the literature, is reputed to be exceedingly uncommon. Evans (1948) states that he has not met with it in aortic stenosis, and Kumpe and Bean (1948) record "gallop rhythm" in only 5 of their 107 cases. The finding of unquestionable triple rhythm in four cases in the present series is therefore of importance in that this sign should not influence the observer against a diagnosis of aortic stenosis. Possibly this increased incidence reflects a greater interest in triple rhythm in recent years, stimulated by the work of Evans (1943).

Special Investigations

Electrocardiography contributed little to the diagnosis of the valvular lesion, although several tracings suggested a diagnosis of aortic stenosis retrospectively and showed the distinctive graph described by Evans (1948). Electrocardiography was of most value in elucidating rhythm disorders and in revealing conduction defects, which were frequent.

Auricular fibrillation is often regarded as rather rare in aortic stenosis (Contratto and Levine, 1937; Dry and Willius, 1939; Scherf and Boyd, 1948); yet it was present in five of the present cases. A comparable incidence is noted by Kumpe and Bean (1948). It is considered, therefore, that the presence of auricular fibrillation should not weigh too heavily against the diagnosis of isolated aortic stenosis on the one hand, or demand too strongly the coexistence of mitral stenosis as an explanation of the rhythm disorder on the other. The finding of left bundle-branch block in one-quarter of the cases supports the view of Berk and Dinnerstein (1938) that left bundle-branch block is found more often in aortic stenosis than in any other condition, with the possible exception of hypertensive disease.

In this series radiology was of limited diagnostic value. There is no doubt, however, that routine screening of the heart and a careful search for calcification of the aortic valve, using a proper technique, is a most valuable diagnostic procedure (Sosman and Wosika, 1933; Parkinson, 1949). Sosman (1939) has demonstrated the remarkable precision that may be achieved

in the diagnosis of intracardiac calcification, and Parkinson (1949) states that calcification of the aortic valve is so rarely absent in aortic stenosis that its demonstration radiologically is comparable in diagnostic worth with enlargement of the left auricle as evidence of mitral stenosis. Calcification of the aortic valve was observed in 26 of 32 cases of aortic stenosis reported by Contratto and Levine (1937), who state that this fluoroscopic sign was always indicative of significant aortic stenosis. The value of tomography has been shown by Davies and Steiner (1949), who report 14 cases of aortic stenosis all diagnosed by tomographic record of the calcified valve.

If every case of suspected heart disease with a rough aortic systolic murmur were screened by the proper technique, or submitted to tomography, few cases of established aortic stenosis would be missed clinically. Routine investigation in this manner would also serve to prevent unwarranted cardiac invalidism through the making of a diagnosis of aortic stenosis in such conditions as hypertension and aortic sclerosis, which are often accompanied by an aortic systolic murmur.

The Terminal Illness

The onset of symptoms, whether cardiac or cerebral, carries a grave prognosis. The course of the illness is then relentless; the response to treatment is poor, and death follows from heart failure within two years of the first symptom. The average survival following the first symptom in this series (14 months) is comparable with the findings of Contratto and Levine (1937) that the duration of life after the onset of dyspnoea was 23 months, of syncope 9.1 months, and of oedema 9.3 months. Rapidly progressive left ventricular failure soon follows symptoms of giddiness, syncope, cardiac dyspnoea, or anginal pain in most cases, although syncopal attacks sometimes occur years before the terminal illness. Patients rarely survive a second attack of acute heart failure. This march of events, so clearly demonstrated by the present series, confirms the experience of McGinn and White (1934) and contrasts sharply with the usual progress of heart failure from mitral stenosis or hypertension.

Familiarity with the natural history of aortic stenosis, once symptoms develop, may assist diagnosis, especially when the expected signs of the valvular lesion are lacking. In the absence of gross coronary artery disease, hypertension, and aortic incompetence, the rapid development, in an elderly subject, of heart failure which is peculiarly resistant to treatment should suggest the diagnosis, especially if the rhythm be normal. If in addition there is a history of syncopal attacks and nocturnal dyspnoea, and a harsh basal systolic murmur is present, aortic stenosis is likely. During the terminal phase the occurrence of sweating attacks and pallor, which may be associated with mental confusion and maniacal symptoms, or even the manner of death, may give a clue to the diagnosis when this has remained in doubt for want of better evidence.

Sudden death in hospital practice is perhaps too often attributed to pulmonary embolus or cardiac infarction. The recognition that one in every five cases of aortic stenosis ultimately dies suddenly or unexpectedly may permit a tardy but correct clinical diagnosis in some cases of obscure heart disease.

Accuracy of Clinical Diagnosis

A correct clinical diagnosis in 52% of this series compares favourably with corresponding figures of 52.9% (Thompson and Levine, 1936), 33% (McGinn and White, 1934), 25% (Karsner and Koletsky, 1947), and 24% (Kumpe and Bean, 1948). The present figure, although encouraging, is by no means satisfactory.

In six of the cases incorrectly diagnosed in life but with grossly calcified valves, fluoroscopy could have settled the diagnosis, although it is admitted that some of the patients were too ill for this to be carried out. Closer attention to a long history of repeated attacks of fainting and giddiness in one patient with a harsh basal systolic murmur but a normal blood pressure should have led to recognition of the valvular lesion. A short history of heart failure in three patients with normal blood pressures and basal systolic murmurs, but without electrocardiographic evidence of cardiac infarction, who developed acute mental symptoms during the final illness which terminated suddenly, offered enough clinical evidence for a confident diagnosis of aortic stenosis

Summary

Significant aortic stenosis, almost always calcareous, is a common clinical and pathological entity. In this study, it occurred in 1.8% of routine necropsies.

In 25 proved cases of isolated calcareous aortic stenosis, heart failure and infective endocarditis were the commonest causes of death. In only three cases was aortic stenosis an incidental post-mortem finding.

A correct clinical diagnosis was made in just over half of the cases. On the basis of the classical signs of a slowly rising pulse, an aortic systolic murmur and thrill, and an absent second sound, less than one-sixth of the cases would have been recognized clinically.

Reasons are given to show that considerably more than half the reported cases might have been correctly diagnosed in life. A more careful evaluation of harsh aortic systolic murmurs, and demonstration by fluoroscopy of grossly calcified aortic valves, could have settled the diagnosis in some cases; a closer study of the natural history of the disease after the onset of symptoms should have directed attention to the valvular lesion in others.

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SUBACUTE BACTERIAL ENDOCARDITIS DUE TO H. PARA-INFLUENZAE AND STR. VIRIDANS

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Streptococcus viridans is the infecting organism in most cases of subacute bacterial endocarditis; haemophilic bacteria occur among the rare causal organisms, and of these *Haemophilus para-influenzae* (Rivers, 1922) is probably the most common (see Miles and Gray, 1938; Craven, Poston, and Orgain, 1940). A case due to this organism was first reported in Britain by Russell and Fildes (1928). Recently this condition has been recognized on a number of occasions and treated beneficially with sulphadiazine (Hunter and Duane, 1946), penicillin and sulphamerazine (Priest *et al.*, 1947), and streptomycin (Briggs and Flinn, 1947; Paul, Bland, and White, 1947; Massel *et al.*, 1948; Olinger, 1948).

Endocarditis due to mixed infection with various organisms has also been described; two cases due to mixed infection with *Str. viridans* and *H. para-influenzae* have been reported (Orgain and Poston, 1942; Olinger, 1948); Olinger's case responded to combined penicillin and streptomycin therapy. A similar case is reported here.

Case Report

An unmarried 27-year-old female bank clerk was admitted to the Western Infirmary, Glasgow, on February 11, 1950, with pyrexia of unknown origin. Over the previous year she had suffered from mild nervousness and occasional anorexia associated with minor emotional upsets, and, when questioned, admitted to having had more dyspnoea on effort than usual. She was otherwise well until the night of December 28, 1949, when she was sleepless from headache and nausea. During the next few days she developed anorexia, some constipation, and pyrexia, with shivering during the day and fever at night; her urine was dark and concentrated, and the output diminished. There was no ankle swelling or palpitation, nor were cardiac murmurs heard during diastole. In the six weeks before admission she was treated with sulphonamides, aspirin, and phenobarbitone without benefit. She gave a history of measles, mumps, whooping-cough, chicken-pox, and tonsillectomy in childhood, but not of rheumatic fever or diphtheria.

On admission she was nervous, with a fine tremor of the hands; her skin was hot and dry; her temperature was 101° F. (38.3° C.), respirations 24, and pulse 116, regular; the blood pressure was 110/50. The heart was slightly enlarged to the left, and a well-marked presystolic murmur and a blowing systolic murmur were audible at the apex. A third heart sound was present. The tongue was coated and there was a small area of tenderness to the right of the umbilicus. The urine contained a few red cells and slightly increased urobilinogen. Blood examination showed: Hb, 75% (Sahli); red cells, 4,600,000 per c.mm.; white cells, 14,000 per c.mm. (polymorphs 79%, lymphocytes 17%, monocytes 4%); slight ring-staining of red cells; E.S.R., 90 mm. in 1 hour (Westergren). The spleen was not palpable and no other abnormalities were detected; salmonella and brucella agglutinations were negative.

Sodium salicylate and sodium bicarbonate, 30 gr. (2 g.) of each, were given three times a day. On February 15, four days after admission, a mid-diastolic murmur was heard at the left border of the sternum for the first time, and the patient complained of pain in the tips of her fingers, although no lesion was visible. The temperature was remitting between 100 and 103° F. (37.8 and 39.4° C.). Blood was withdrawn for culture, and penicillin therapy, 2,000,000 units daily in three-hourly injections, was begun. By February 19 *Str. viridans* and unidentified Gram-negative filaments were reported in the blood culture. The dosage of penicillin was increased to 5,000,000 units daily. Very slight haematuria was still present, but there were no other embolic phenomena; the cardiac condition remained unchanged. By March 14 the temperature had fallen to 98.8–100° F. (37.1–37.8° C.) and the patient's general condition had improved, although the haemoglobin level had fallen to 55% (Sahli). On March 22 the temperature rose again to 102° F. (38.9° C.) and a hot tender swelling appeared at the site of a penicillin injection; this subsided quickly and then the temperature fell to 99° F. (37.2° C.). On March 30 one pint (570 ml.) of packed cells was given intravenously on account of the anaemia. Penicillin therapy was stopped on April 6, the patient having received 224,000,000 units.

On the next day the temperature began to rise and ran a remitting course between 101 and 102.8° F. (38.3 and 39.3° C.), and some petechiae were seen. In a blood culture taken on April 10 a pure growth of Gram-negative filaments was again found and "aureomycin" therapy was started, 1 g. daily for four days; by that time the organism was identified as a haemophilus sensitive to streptomycin, which was therefore substituted (2 g. daily) for aureomycin, the latter being still scarce. The temperature at once settled and remained normal for a week. By April 24 the mid-diastolic and presystolic murmurs were less intense. On April 28 a small, hot, red swelling appeared over the radial artery of the left wrist; it vanished after a few days and is considered to have been embolic in origin. A subsequent rise in temperature disappeared as soon as the streptomycin was stopped on May 1, and is thought to have been a drug reaction. A total of 26 g. of streptomycin was given.

On May 3 no mid-diastolic murmur was audible. The E.S.R. was 13 mm. in 1 hour (Westergren); the pulse rate returned to normal; the haemoglobin was 80%; blood cultures were sterile; the general condition was excellent; the presystolic murmur had become minimal; and the patient was discharged on June 3.

When examined on July 6 she was found to be remarkably well. Exercise tolerance appeared as good as before her illness. A blowing systolic murmur of moderate intensity was present at the apex, and on reinforcement a typical presystolic murmur could be heard; no enlargement of the heart was detected.

Laboratory Findings

In the first blood cultures* (February 15) *Str. viridans* and a Gram-negative organism grew; the latter was lost before identification. Further cultures on February 15, 17, 21, and March 4 were sterile.

In cultures taken some seven weeks later (April 10, 11, and 13) there appeared, after 96 hours' incubation, fluffy colonies about 1–2 mm. in diameter, lying on the surface of the sedimented cells. The colonies consisted of tangled masses of long thin Gram-negative filaments. Subcultures on 10% horse-blood agar, after 24 hours' incubation, showed minute, non-haemolytic, seemingly smooth, transparent colonies which in 48–72 hours reached 0.5 mm. in diameter and became more opaque and rough with tiny ridges; they were tough and difficult to break up. In meat-extract broth with 10% horse blood, growth was similar to that of the original blood cultures, with small fluffy colonies tending to adhere to the sides of the tubes. Both with solid and with fluid media the organism was highly pleomorphic, ranging in size from cocco-bacillary forms to long thin thread-like filaments, staining fairly evenly but rather faintly with dilute fuchsin, aerobic, non-sporing, non-motile, and non-acid fast.

*Three bottles of media were always inoculated with blood (see Browning and Mackie, 1949).

No growth occurred in ordinary media or media enriched with glucose, starch, human serum, human plasma, or horse plasma, or on Loeffler's inspissated serum.

As growth had been obtained only in the presence of blood, the organism was assigned provisionally to the *Haemophilus* group and the growth requirements were investigated in some detail. On "chocolate blood agar" (heated to 80° C.) growth was slower and weaker than on blood agar; no growth occurred on autoclaved blood agar. On the other hand, the organism grew on ordinary agar around colonies of staphylococci, and in broth to which staphylococcus filtrate was added; abundant growth took place in media containing 10% yeast extract. Thus the organism required the presence of the V or co-enzyme factor, and was independent of the X or haematin factor. It was therefore identified as a non-haemolytic *H. para-influenzae* (Valentine and Rivers, 1927).

Fermentation tests were carried out in peptone water with 10% yeast extract—prepared according to the method of Miles and Gray (1938)—which by itself does not split saccharose or maltose. The organism grew well in this medium and produced acid, without gas, from glucose, saccharose, and maltose, but not from lactose, mannitol, or dulcitol. No change occurred in litmus milk, and indole was not produced.

This organism died out on agar plates in 48–72 hours but survived for 11 weeks in blood-culture bottles which, after five days' incubation at 37° C., were left at room temperature. It survived heating to 56° C. for five minutes, but not for 10 minutes.

The organism was completely resistant to penicillin (10 units per ml.), was highly sensitive to streptomycin in the "ditch test," and in fluid media growth was inhibited by 1.6 μg. of streptomycin per ml. of medium.

On May 22 the patient's serum was tested for antibodies. Miles and Gray (1938) reported agglutination of *H. para-influenzae* by their patient's serum to a titre of 1 in 90, but stressed the difficulty of preparing a stable suspension of the organism. The same difficulty, due to roughness of the colonies, was experienced with our strain. Unsuccessful attempts were made to emulsify colonies in saline by raising the *p*H to 8.2. Fine suspensions of organisms or fragmented organisms were obtained by grinding colonies in a mortar and slowly adding saline or ox bile; gentle centrifugation was necessary to remove unbroken clumps of organisms. Such suspensions were agglutinated markedly at 56° C. by the patient's serum to a titre of 1 in 100, but slight sedimentation also occurred in higher dilutions of the serum and in control tubes. The most satisfactory results were obtained by the method for suspending tubercle bacilli used in the Pasteur Institute. The colonies were ground in olive oil, and 0.85% NaCl was slowly added to make an emulsion. Left for three hours, the emulsion separated, and between the oil and the sediment of unbroken remnants of colonies there was a fine suspension of organisms completely stable at 56° C.; this was agglutinated by the serum overnight at 56° C. to a titre of 1 in 250, and to the same titre but rather more slowly at 37° C.

Discussion

Proof that a case of endocarditis is due to a particular organism is not easily obtained during the patient's life; repeated positive blood cultures are usually taken as significant. It seems reasonable to assume that the unidentified bacterium in the first blood culture was the *H. para-influenzae* grown later on three separate occasions. The repeated presence of this organism in the blood stream, its disappearance after antibiotic therapy, to which it was sensitive, accompanied by the disappearance of the pyrexia and marked clinical improvement of the patient, all point to the organism being a causal agent of the disease. *Str. viridans* was grown only from the first blood culture, but thereafter intensive penicillin therapy probably precluded the possibility of its subsequent isolation. However, definite clinical improvement and lowering of the pyrexia during the penicillin therapy (to which the haemophilus was completely resistant in *in vitro* tests) led us to believe that the streptococcus was also a causal agent.

Summary

The clinical and laboratory findings are given of a case of subacute bacterial endocarditis apparently due to a mixed infection with *H. para-influenzae* and *Str. viridans*: the successful treatment of the case is described.

The unusually long (11 weeks) survival of *H. para-influenzae in vitro* and the method of preparing a stable suspension are thought to be interesting laboratory findings.

We have to thank Dr. W. R. Snodgrass, under whose care the patient was, for much help on the clinical aspects of the case.

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LEG-LENGTHENING*

BY

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Since shortening of the lower limb is a common complication of many conditions, attempts have naturally been made from time to time to correct this deformity by operative means. Little success, however, attended these efforts until the principles of skeletal traction were well established. Putti (1921) published his paper on operative lengthening of the femur; then in 1927 Abbott described his method of tibial elongation, and all subsequent methods have been based on his work. His operative technique was complicated, and involved a good deal of soft-tissue division, and the distraction apparatus used had no provision for preventing secondary deformities.

The present paper is based on 101 personal cases.

Indications and Contraindications

The indication for leg-lengthening is a shortening exceeding 1½ to 2 in. (3.75 to 5 cm.) with a mobile pelvis, or exceeding 1 in. (2.5 cm.) if no compensation is possible by pelvic tilting.

*Read to the Section of Orthopaedics at the Annual Meeting of the British Medical Association, Liverpool, 1950.

Contraindications are: (1) faulty nutrition of the short limb; (2) shortening so great that amputation and the fitting of a prosthesis would be the better plan; (3) active or recently active bone or joint disease; (4) age—only adolescent and young adult patients are suitable; and (5) poor control—though it is sometimes worth while lengthening a completely flail limb to be rid of a heavy and unsightly high boot.

Choice of Operation

There are three possible operative methods of limb equalization: (1) limb-lengthening; (2) limb-shortening; and (3) arrest of epiphysial growth. There is no doubt that lengthening is by far the most difficult technically, and is subject to hazards which have to be guarded against very carefully, yet it offers advantages which the other methods do not, and the patient or his parents often find it to be the most attractive course.

For an individual who is going to grow tall, controlled epiphysial arrest certainly seems to be the ideal procedure, and I have already started to treat a number of cases by epiphysial stapling. In the majority, however, full or nearly full growth has already been attained, and there will always be a number in whom the chance of slowing growth in the longer limb will have been missed.

There remains the choice of lengthening or shortening, and I have found that, when the alternative is offered, lengthening is chosen even after the comparative simplicity of shortening is stressed. This is because the one offers the possibility of a return to a condition more approaching the normal, while the other is regarded by the patient as a mutilation. I came across this attitude very strongly expressed by a girl who had one leg abnormally long because of a haemangiomatous condition, the short leg being the normal. Although a tall girl, she very firmly declined to have the abnormal limb shortened. Finally, many persons having a short lower limb are stunted in growth, and in them a further decrease in total height is a serious matter. Limb-lengthening must then be the first choice to consider.

Operative Technique

Previous writers have drawn attention to the difficulties attending lengthening, to the hazards involved, and to some of the calamities which may result. Compere (1936) made a list of possible complications. McCarroll (1950) discussed the severe complications which certain surgeons encountered. In my opinion nearly all the difficulties and many of the risks enumerated are due to interference with the blood supply to the limb or to the separated bone fragments. This results almost entirely from the extensive soft-tissue dissection which is carried out by those who believe that the soft tissues will not stretch or will be permanently injured during stretching. This is not so, and all that is theoretically necessary is to divide the bone and then gradually to separate the fragments. Everything else will stretch, given sufficient time and a distracting force that is strong enough. The operation should therefore be confined to a Z-shaped or oblique osteotomy and to the application of the distracting apparatus.

The design of the apparatus is of great importance; in fact, the success and ease of the whole undertaking depend on it. It should do three things: afford a means of applying controlled and progressive distraction to the fragments; maintain good alignment; and prevent the development of secondary deformity. As lengthening proceeds, especially of the tibia, the tension in the soft tissues varies, so that deformities tend to develop at the ankle and tarsal levels. In all but the first few of the series now described the limb has been enclosed in a firmly fitted plaster extending from waist to toes in femoral and from mid-thigh to toes in tibial lengthening. This plaster resists the secondary forces set up and transfers them to skin surfaces, but the pressure must be well distributed and sores prevented by adequate padding and good moulding.

In tibial lengthening the apparatus used has not been modified during the past 10 years. It consists of a carrier supporting four stirrups in pairs, which can be separated from each other by turning a screw. The distraction is progressive because the stirrups are elastic and accumulate the distracting force, applying it gradually to the limb. At least four stirrups are needed, since there is a tendency for the tibia to bow forwards as it lengthens, as all the muscles are behind its axis. Further support is supplied by plaster struts under the heel and the mid-thigh.

In femoral lengthening, contrary to McCarroll's experience, there is little difficulty in maintaining alignment. Only two stirrups are used, situated as close to the osteotomy as possible, and alignment is maintained by incorporating telescopic tubes in the surrounding plaster spica (see Fig. 1).

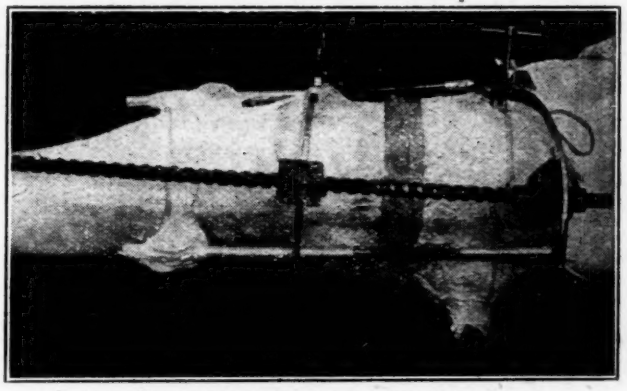

FIG. 1.—Distraction apparatus in femoral lengthening.

The operative technique in both operations is similar. An incision of the required length is made down to the periosteum, the oblique cut is outlined by drill-holes placed close together, piercing both cortices, and the bone is then divided by an osteotome. As the near cortex is divided the back cortex breaks along the line of holes, so that the periosteum remains relatively intact. Below the knee the fibula is divided transversely at one or two levels. The tendo Achillis has been lengthened at this stage only when an equinus deformity has existed before the operation. Kirschner wires to fit the stirrups are inserted above and below the osteotomy—in the tibia all in one plane, in the femur in planes so as to avoid the main vessels and nerves—and the two may even be at right angles to each other without adding any difficulty to the application of the distraction apparatus.

Management of Distraction

Distraction is started immediately, and proceeds at the rate of about $\frac{1}{16}$ in. (1.6 mm.) a day. It is regulated largely by the patient's reactions. At first no pain is felt, apart from that due to the operation, and this is

minimized by the completeness of the fixation. Then, as the tension in the soft tissues increases, an aching comes on an hour or so after the apparatus is adjusted; but this soon passes off. If any pain is complained of at one of the sites subject to skin pressure—and in tibial lengthening these are the sole of the foot, the tip of the external malleolus, the back of the heel, and about the head of the fibula—distraction is stopped at once and the site of the pain investigated by cutting a window in the plaster. A little reddening of the skin may be observed, and the trouble is stopped by an adjustment of the padding; if this is not done the pain soon ceases, but a plaster sore results. It is unusual for this complication to arise until an increase in length of about 2 in. (5 cm.) is reached.

At about the same time some weakening of power in the extensors of the toes may be noticed. This is due to failure of conduction in the external popliteal nerve, which is the most sensitive of all the soft structures to lengthening. Experience has shown that within the limits of reasonable lengthening this is only a temporary change. There is a rapid improvement if distraction is stopped or slowed, but if this is not done and a complete paralysis of the extensor muscles results, recovery is usually complete by the time the fragments have united, and in no case has any permanent loss of function been noted. This effect on the nerve may occur after 3 in. (7.5 cm.) of tibial or 2 in. of femoral lengthening has been gained.

FIG. 2.—Radiograph in a case of tibial lengthening (on account of Ollier's disease) showing separation of the fragments and the beginning of new bone formation.

Radiographs are taken at intervals during this period. After the first month there is usually evidence of new bone being laid down in streaks parallel with the axis of the bone and bridging the gap, and it would seem that this bone grows from the periosteum (Fig. 2). Since it is known that a good deal of the periosteal cuff is intact, in the few cases where one of the tongues of the osteotomy has broken, one has not hesitated to carry on, and union has not been unduly delayed.

When the required length has been attained the limb is left undisturbed on the apparatus until there is enough new bone to support the osteotomy; then, before union is firm, the apparatus is dismantled and the limb enclosed in a complete plaster. This affords an opportunity of making slight corrections in the alignment. It is usual to find that the normal bowing of the tibia has been lost, and the relation of the planes of the knee-joint and ankle-joint may need adjustment. The patient can now be got up on crutches. Full weight-bearing is not allowed until the osteotomy is firm both clinically and radiologically (Fig. 3). The average time before this stage is reached is five months in femoral cases and six and a half months in tibial cases. The reason why the tibia takes longer to consolidate is probably because greater increases in length have to be obtained in that bone.

One difficulty has been to maintain muscle integrity. Voluntary movements of the toes and contractions of the quadriceps are encouraged from the start. As muscle tension rises movement becomes harder, and it is not always easy to distinguish between difficulty in extending the toes due to failure of nerve conduction and that due to the increased tension in the muscles. As soon as distraction is stopped improvement is rapid, and no case has shown any ultimate loss of muscle power. There is a good deal of apparent muscle-wasting, but it must be borne in mind that the muscles have been stretched, so that the loss of bulk is not so great as it may seem.

FIG. 3. — Radiograph showing final result in the case illustrated in Fig. 2.

Possible Complications

Mention has already been made of some of the possible complications. Some of these are so serious that they imperil the life of the patient, or they may make the final state of the patient worse than before operation. This subject is so important that it is considered advisable to discuss all the possible complications catalogued by Compere (1936).

Stretch Paralysis of Sciatic or External Popliteal Nerve.—This complication has occurred in one-seventh of the present 101 cases. In the majority it has been transient, lasting at the most for a few weeks, but in one case paralysis

persisted for seven months; here, however, muscle power recovered fully.

Increased Weakness of Lengthened Muscles in Old Cases of Poliomyelitis.—This certainly occurs and is difficult to assess. In my experience a return to previous muscle power occurs within a few months.

Fracture of Osteotomy Fragment.—This happened five times in the present series. With the operative technique described it seems to be of little importance, and union has not been delayed by this complication.

Malunion.—There were no cases of gross malunion. Slight loss of tibial bowing occurred in a few, and one case showed slight valgus bowing.

Delayed Union and Non-union.—In eight cases union was delayed over seven months and in one case over 12 months. One case of non-union required secondary bone-grafting.

Osteomyelitis from Wound Infection and Lighting Up of Silent Focus.—In two early cases of tibial shortening due to osteomyelitis single flake sequestra separated during the period of consolidation. Since chemotherapeutic agents have been available no case of bone sepsis has occurred.

Traumatic Arthritis and Limitation of Movement in Knee.—Transient stiffness is usual in femoral lengthening. Only two cases had less than 90 degrees flexion a year after operation, and both these had more than 60 degrees. No trouble was experienced in tibial lengthening.

Late Fracture.—This complication was not experienced until 90 cases had been done, but it has since occurred in two. Union of the secondary fracture has been rapid, and in one case a little additional length was obtained.

Pressure or Stretch Necrosis of Skin in Zone of Lengthening.—This may happen in tibial cases when an increase in length of over 3 in. (7.5 cm.) has been obtained, but is not a serious complication and does not delay healing.

Necrosis of Bone Due to Excessive Subperiosteal Stripping.—The technique described prevents this complication.

Malposition of Foot Due to Rotation During Lengthening.—The present technique has prevented this except on two occasions.

Circulatory Disturbance with Prolonged Oedema in the Lengthened Limb.—This has not been encountered.

Displacement of Head or Distal End of Fibula when this Bone is Lengthened Less than the Tibia.—Displacement of the head occurs occasionally. No disability results, and it has no influence on external popliteal nerve paralysis. Upward displacement of the distal end has occurred once; it did not lead to disability.

Protrusion of Osteotomy Fragment Through the Skin.—This may occur in tibial lengthening, but can be avoided by a slight backward angulation of the fragments before distraction.

The following complications were not mentioned by Compere.

Secondary Deformities Due to Mounting Muscle Tension.—These can all be overcome by the technique described, except for an occasional equinus deformity which may need a subsequent stretching or lengthening of the tendo Achillis.

Pressure Sores.—These may occur if the patient's complaints are unheeded.

Pins Pulling Out.—All pins or wires should be inserted through compact bone.

Gangrene.—This complication, which has been described by McCarroll (1950), has not to my knowledge occurred in this country, and seems to be due to far too rapid distraction. No vascular complication has been experienced in the present series.

Results

So far 101 cases have been submitted to this operation (see Table)—54 to tibial lengthening (see Fig. 4) and 47 to femoral lengthening (see Fig. 5). A detailed analysis of the first 87 cases has already been published (Allan, 1948).

Diagnoses in 101 Cases in Which Leg-lengthening Operations Have Been Performed

Tibia and Fibula	No.	Femur	No.
Infantile paralysis	30	Tuberculous arthritis of hip	18
Congenital shortening	7	Malunited fractures	6
Tuberculous arthritis of hip	5	Tuberculous arthritis of knee	5
Osteomyelitis of tibia	3	Congenital shortening	5
Osteomyelitis of pelvis	1	Osteomyelitis of femur	5
Tuberculous arthritis of knee	1	Infantile paralysis	5
Ollier's disease	1	Septic arthritis of hip	1
Hemiplegia	1	Unreduced congenital dislocation of hip	1
Venous angioma	1	Congenital scoliosis with fixed pelvic obliquity	1
Rachitic shortening	1		
Malunited fracture	1		
Epiphysial injury	1		
Radium burn	1		
Total	54	Total	47

In one case with over 6 in. (15 cm.) of shortening the femur was lengthened twice and the tibia once. In all about 7 in. (10.5 cm.) of lengthening was obtained, but as the procedure was started when the child was 13 the normal leg was still growing, and at the end a shortening of 1 in. (2.5 cm.) persisted. There was an interval of about a year between each stage. Only when the tibia was lengthened 2½ in. (6.25 cm.) did the external popliteal nerve suffer, and it recovered rapidly. In another case both femur and tibia were done with a two-year interval, giving a total of 4½ in. (11.25 cm.). In a boy with 8 in. (20 cm.) of shortening following tuberculous arthritis of the hip, the legs were equalized by

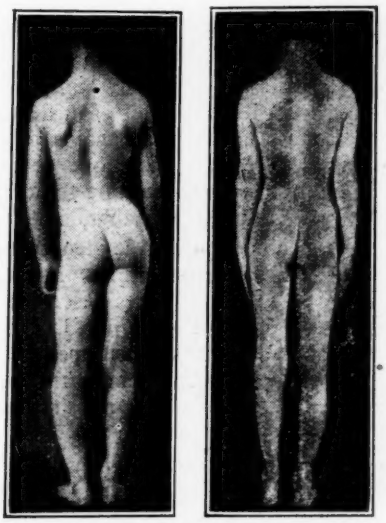

FIG. 4.—A patient in whom tibial lengthening has been carried out, photographed before and after operation.

FIG. 5.—A patient in whom femoral lengthening has been carried out, photographed before and after operation.

lengthening the short limb 5 in. (12.5 cm.)—2 in. (5 cm.) above and 3 in. (7.5 cm.) below the knee-joint—shortening the normal tibia by 2 in., and compensating for the remaining inch by pelvic tilting. The greatest gains in length have been 3½ in. (8.75 cm.) in the femur (one case) and 4½ in. in the tibia (two cases).

Experience with the recent cases has not differed very much from that previously reported, except that the complication of secondary fracture, not encountered before, has happened twice without, however, any loss of length already gained, but with a delay of three months in each case before final recovery. It is possible, too, that in a case not included in this series a paresis of some of the muscles supplied by the anterior tibial nerve which occurred immediately after the operation, before distraction started, was due to direct transfixion of a nerve branch by one of the distracting Kirschner wires. No tourniquet was used. This complication should be avoidable by placing these wires well forward through the crest of the tibia.

The average lengthening in the whole series is 2½ in. (6.25 cm.) in the tibia and 1¾ in. (4.4 cm.) in the femur.

Conclusion

Gains in length in both tibia and femur up to 2 in. are possible without any complication, transient or permanent. Beyond that, transient complications occur, and must be weighed against the desire to gain more length. With the technique described no difficulty has been found in maintaining femoral alignment, and little in maintaining tibial alignment.

The choice between leg-lengthening and leg-shortening is not an easy one to make. It may be pointed out, however, that the difficulties described do not arise suddenly and can often be anticipated. The distraction stages of the operation may be stopped at any time, before any temporary or permanent harm is done, and the operation of shortening the opposite limb still be carried out.

Summary

The indications for and against leg equalization are summarized, and the choice of operative procedures is discussed.

The operative technique and the management of distraction in leg-lengthening are described.

The possible complications of leg-lengthening are discussed.

The results in 101 personal cases are presented.

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The Food and Agriculture Organization (F.A.O.) and the Government of Peru have signed an agreement to improve nutrition and bring about more adequate diets in Peru by providing a nutrition consultant who will help to plan and organize dietary surveys and biological work in nutrition; by providing four fellowships to technicians already working in the field of nutrition; and by the purchase and transport of equipment and supplies for the animal experiment laboratory at Lima. The present agreement is the twenty-first which F.A.O. has made, and Guatemala, Costa Rica, Uruguay, Ecuador, Honduras, Colombia, and Haiti are already included.

BONE-SHORTENING FOR INEQUALITY OF LEG LENGTHS*

BY

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In considering the treatment of inequality of leg lengths we must first decide what degree of inequality calls for surgical measures. Up to ¼ in. (2 cm.), a person of average stature can ignore the discrepancy; up to 1½ in (3.75 cm.) the inequality can be readily dealt with by a lift of one heel and a dropping of the other. As a rule surgery need not be considered until a discrepancy of over 1½ in. has occurred or is anticipated. Warren White (1947) wisely stressed the unimportance of a slight discrepancy in length: a limp is usually due to the muscle weakness, and he reports a shortening of 2 in. (5 cm.) with no limp. In his opinion the hazards of the compensatory scoliosis have also been overemphasized. Two further points need to be stressed: first, where a patient has to wear a calliper the elimination of a surgical boot alone does not warrant surgery, and, secondly, all cases need to be carefully documented as regards bone lengths, preferably by accurate radiographic recording.

Risks of Bone-lengthening

The inequality can be corrected by leg-lengthening or leg-shortening; the former is the ideal treatment, and the latter can have an appeal only to the extent that bone-lengthening is regarded as over-ambitious and carrying too great risks. What are these risks? Deformity and sepsis when the bone fragments are not under complete control, delayed union and late fractures, paralyses, vascular trouble with oedema, stiff joints, and weakened muscles are some of those which seem to occur in most series of any size. That this is the present opinion in America is indicated by the following extracts from recent literature. Abbott and Saunders (1939), who have done so much to popularize bone-lengthening, wrote in 1939: "We emphasize that the procedure of bone-lengthening is, and in all probability always will be, a major operation, with the possibility of serious complications." This is a grave warning when applied to a purely elective procedure. Barr (1948) wrote of these procedures: "The operation of femoral lengthening was therefore soon abandoned"; and later, referring to lower-leg lengthening, "It is safe to say that the operation, once reasonably popular, is now rarely done." These remarks may apply more to America than this country, but even the surgeons who favour this form of treatment will admit that serious risks are run, the procedure is lengthy, and convalescence is often protracted—a minimum of six months seems to be required.

Most cases of inequality of leg length result from anterior poliomyelitis, and the weakened muscles cannot be assisted by the additional stretching entailed by leg lengthening. On the other hand, the well-muscled limb with shortening from congenital or other causes unconnected with paralysis, is less suitable for leg-lengthening, allowing of little elongation and being rather more prone to all complications.

*Read to the Section of Orthopaedics at the Annual Meeting of the British Medical Association, Liverpool, 1950.

As a consequence of these risks, many surgeons have turned to surgical shortening as a wiser procedure; but they at once come under criticism for two reasons: (1) the patient's loss of height, and (2) the fact that the elective surgery is performed on the normal leg of a patient already afflicted with a considerable disability in his other leg. Loss of height is humiliating in the true sense of the word—which means bringing one nearer to the ground. To the tall it means little, but to those short in stature it may mean a great deal, and it is certainly of more importance to a man than to a woman. With due regard to all the claims made for leg-lengthening, it would seem, however, that one should practise bone-shortening in all but a small group of patients who either are unwilling or can ill afford to sacrifice any fraction of their height.

Epiphysiodesis

Bone-shortening is usually accomplished by epiphysial arrest during the growth period or by surgical bone-shortening—at any age, but preferably after growth has ceased. Epiphysial arrest can be accomplished by epiphysiodesis—a procedure introduced by Phemister (1933) and of established value—or mechanical retardation of metaphysial growth by staples—a procedure introduced by Blount in recent years and still in an experimental stage. The preliminary report by Blount and Clarke (1949) was very impressive, and an important new method of leg-shortening seems to be available to surgeons; results are but slowly accumulated in such a field, and further reports are awaited with keen interest.

It is very important to estimate accurately the effect of epiphysiodesis. The calculation of expected growth and expected discrepancy in leg length is the basis of the method advocated by Wilson and Thompson (1939), while Warren White (1947) uses a simple estimation that the distal epiphysis of the femur will contribute ½ in. (1 cm.) per annum and the upper tibial epiphysis ¼ in. (0.6 cm.) per annum up to the age of 17 in boys and 16 in girls. Growth varies so greatly with each individual that the simpler method is as likely to give good results as any. Errors are usually on the side of insufficient correction; hence it is rarely advisable to delay epiphysiodesis beyond 11 years in a girl or 12½ in a boy.

A good result may be claimed if the final leg lengths differ by less than ¾ in. (2 cm.) (Straub, Thompson, and Wilson, 1945) and if the shorter leg is the same or reversed. Reported series rarely contain more than one case of over-shortening. This is not only on account of delay in operating but also, as mentioned by Warren White, because little correction occurs in the first year, the stimulation to metaphysial growth being only just counterbalanced by the destruction of the epiphysial plate; and other near-by epiphyses may be stimulated by hyperaemia.

Mention must be made of deformities occurring in limbs on which epiphysiodesis has been performed. While Warren White reports only one case in a large series covering 12 years, Straub, Thompson, and Wilson record a series of 103 operations in which 20.7% developed bony deformity, 10.1% of the latter being severe enough to warrant surgical correction; and Regan and Chatterton (1946) report a series of 36 cases with four (11%) severe deformities. Both groups of authors attribute the deformity to faulty technique resulting in partial failure to close the epiphysial line, and Regan and Chatterton combine repetition of the epiphysiodesis locally with correction of the developed deformity.

Phemister described his procedure thus: "A piece of cortex 3 cm. by 1–1.5 cm. wide is excised, crossing the cartilaginous disk and including 1 cm. of the epiphysis. The sides of the cartilaginous disk anterior and posterior to this are chiselled out to a depth of approximately 1 cm. and the transplant is reinserted with its ends reversed." Most surgeons have modified the operation in the direction of greater thoroughness, and it is certain that the stressing of this point alone will reduce this serious deformity rate to a negligible minimum. The procedure advocated by Wilson and Thompson would appear from their subsequent report (Straub, Thompson, and Wilson, 1945) to be insufficient when applied by the various surgeons doing this procedure at any one clinic.

A more thorough operation (Figs. 1 and 2) is accomplished by removing a block of bone containing a great deal more than the cortex. The full depth of the epiphysial plate will accommodate a narrow spoon or curette, with which to remove the cartilaginous seam and make adequate contact between the approach on the two sides. The use of diathermy completes the destruction of the growing cartilage cells throughout the operative fields. The result is so large an area across which fusion must rapidly occur that the remaining two triangles of epiphysial cartilage are suppressed, and even should they function for a while they would from their very central and symmetrical locations produce no deformity. Epiphysiodesis should be evident radiologically within three months (Figs. 3 and 4).

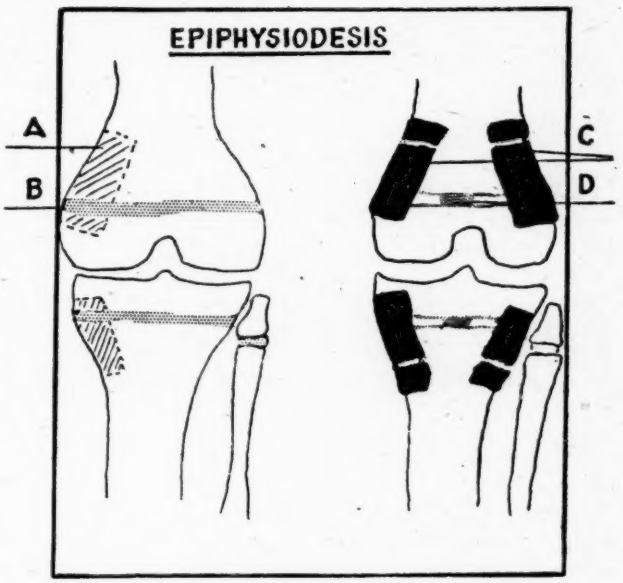

FIG. 1.

FIGS. 1 AND 2.—Diagrammatic representation of operation of epiphysiodesis, with extensive removal of epiphysial plate to avoid all risk of deformity. A, Bone block for removal. B, Epiphysial line. C, Blocks of bone reversed and replaced. D, Removal of epiphysial cartilage from side to side; triangles remain anteriorly and posteriorly. E, Blocks of bone reversed and replaced. F, Remaining triangle of epiphysial cartilage.

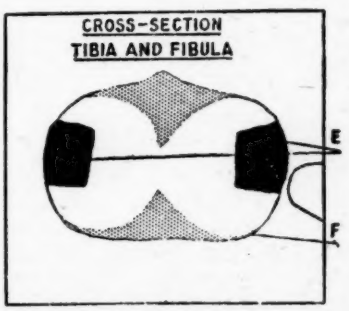

FIG. 2.

Epiphysiodesis can be performed only during the period of active epiphysial growth, but surgical bone-shortening can be done at any age, though it is better delayed until growth has finished. If bone-shortening is carried out during the period of growth, allowance must be made for the fact that the operation itself causes stimulation of growth because of the resulting hyperaemia of the bone. The shortening required will therefore be rather more than that suggested by pre-operation measurements. For any surgeon who practises epiphysial arrest the logical procedure when faced with a patient in an older age group is surely to perform surgical bone-shortening. The outcome is the same whether the loss of stature results immediately or is designed to occur over a period of years.

The procedure of surgical bone-shortening is very much older than leg-lengthening and, according to

FIGS. 3 AND 4.—Good radiological evidence of closure of epiphysial line three months after operation.

Wilson and Thompson (1939), Sayre in 1863 advocated fracturing the femur and allowing the fragments to overlap to the required amount, but Steindler attributes the first operation of leg-shortening to Rizzoli.

Femoral shortening has commonly been performed, and a number of cases are reported in support of Hey Groves's (1931) contention that the femur might be shortened by 25% of its length—4 in. (10 cm.)—with "perfect impunity."

A search of the literature reveals various methods, but a straightforward lateral overlap as advocated by Warren White in 1920 with transfixing screws seems to commend itself because of its very simplicity and freedom from the risk of technical complications, which occasionally occur with the use of such refinements as step cuts or long oblique cuts. With straightforward lateral overlap and transfixing screws the immobilization is excellent, the alignment certain, and the muscular damage minimal, as the operation can be performed through a short exposure. This method of femoral shortening is illustrated in the following case.

Case 1

A girl aged 11 had within a few days of her birth suffered from a haemorrhagic condition leading to the disorganization of her knee and gangrene of a number of her toes. Various operations had been performed on her knee, leaving her at the age of 11½ with an ankylosis of the knee, a closed upper tibial epiphysis, and 4-in. shortening of the leg. The shortening was largely below the knee, but the lower leg was normally muscled—a deterrent even to those who support bone-lengthening. It was decided to equalize the leg lengths by femoral shortening and to equalize future growth by suppression of the upper tibial epiphysis—both these operations to be performed on the normal leg. Her height at the time was 4 ft. 10 in. (147.3 cm.), and at 13½ years she measured 4 ft. 10½ in. (148.6 cm.), her mother's height being 5 ft. 3 in. (160 cm.). In this case, 4-in. shortening was effected through a 5-in. (12.5-cm.) muscle incision, 2 in. (5 cm.) of bone being removed and an overlap of 2½ in. (6.3 cm.) allowed owing to the obliquity of the saw cuts (Fig. 5). Although we were operating on 8 in. (20 cm.) of femur, the muscle incision was no longer than 5 in., the full exposure of the two pieces of femoral shaft being delayed until overlapping was being effected. This procedure proved simple, and there was not much shock. No form of external immobilization was used.

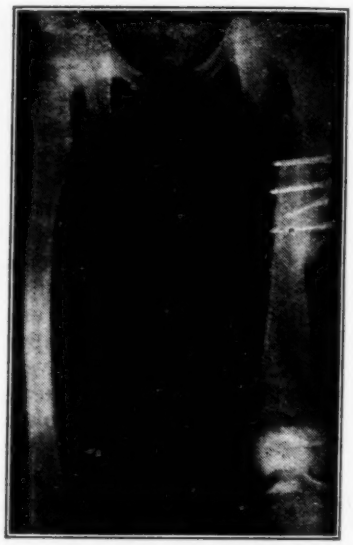

FIG. 5.—Case 1. Showing 4 in. (10 cm.) of shortening by resection of 2 in. (5 cm.) of bone, 2½ in. (6.3 cm.) overlap, and transfixing screws.

Hey Groves (1931) wrote that "it is remarkable how the slack of 4 in. of muscle is taken up within a few months and the full muscular power of the leg regained." This proved to be the case in this girl. Convalescence was complicated by the performance of an upper tibial epiphysiodesis (Fig. 4) seven weeks after the femoral shortening, so that one is not able to quote a date on which she succeeded in straight leg-lifting—a landmark in the recovery of strength in the quadriceps muscle. The joint movements and muscular control were quite unimpaired after a lapse of five months.

The features of this case are: (*a*) the presence of an ankylosed knee on the short leg, allowing of the whole 4 in. being taken from the femur, although both femur and tibia contributed to the shortening; (*b*) the well-muscled short leg, making leg-lengthening a greater hazard than in the more usual case with paralysis; (*c*) the simplicity of the procedure, with minimal risk of complications and a quick result.

Another technique of femoral shortening which can be recommended is illustrated in Case 2. Femoral shortening should be practised high in the shaft, and the use of a Blount plate gives good fixation after such an operation.

Case 2

The patient, a woman with severe Still's disease, had a stiff knee on the short leg, allowing of the shortening being effected entirely in the femur. A corrective osteotomy was required on the long leg as well as 4 in. of shortening, and both procedures were performed in the femur just below the great trochanter; fixation was effected by a Blount plate. Leg equalization was done in this case without immobilization of joints—a very necessary precaution in a case of Still's disease. The patient was walking again within two months of the operation.

Surgical bone-shortening can also be performed in the tibia either by resection transversely and plating, or by resecting obliquely and using screws transversely placed to fix the bone ends.

Summary of Conclusions

Where an inequality of leg length of over 1½ in. is present or is to be anticipated one may arrive at the following conclusions.

1. Bone-shortening is the preferable approach to all cases with the exception of the few who are unwilling or who can ill afford to sacrifice any height.

2. Some surgeons seem far more willing to practise leg-shortening by epiphysiodesis than to attack an older patient by surgical bone-shortening, logically the equivalent operation for an older age group.

3. A very thorough technique is required in epiphysiodesis to avoid deformities, and a more extensive operation than that advocated by Phemister is therefore described.

4. Epiphysiodesis is often performed at too late an age for the desired results to be obtained.

5. Surgical bone-shortening is a safe procedure, and certain and quick in its results—considerable attributes in purely elective surgery.

6. Surgical bone-shortening is preferable in the femur, and two methods are advocated: (*a*) straightforward lateral overlap with transfixing screws; and (*b*) excision of a segment below the lesser trochanter and fixation with a Blount plate.

7. Two further examples of a 4-in. femoral shortening with full return of knee movement and control within three to five months are reported.

In spite of the more challenging nature of leg-lengthening, an attempt has been made to demonstrate that leg-shortening has more to recommend it. Its adoption as the wiser procedure is advocated in most cases presenting with leg inequality sufficient to warrant surgery yet too old for treatment solely by epiphysial arrest.

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The New York Academy of Sciences, the fourth oldest scientific society in the United States—it was founded under a different name in 1817—recently elected a number of new foreign honorary life members, bringing the total of scientists so honoured in its 134 years of existence to 66. Among this latest addition to the roll were several medical men: Professor C. H. Best, of Toronto, co-worker of Banting in the first preparation of insulin and an authority on metabolism; Dr. J. B. Collip, well known for his work on the parathyroids and mineral metabolism; Sir Frank Burnet, of Melbourne, the great authority on virus diseases; and Professor Bernardo Houssay, of Buenos Aires, 1947 Nobel prize-winner in medicine and biology, who has worked on a wide front in endocrinology, and particularly on the pituitary in diabetes and on experimental hypertension. The other scientists were Professor W. T. Astbury, of Leeds (biophysicist), Professor Harold Jeffreys, of Cambridge (geophysicist and astronomer), Professor N. V. Sidgwick, of Oxford (organic chemist), Professor H. R. Kruyt, a Dutch physical chemist, Dr. Eduardo Cruz-Coke, a Chilean biochemist, and Professor J. Runnstrom, of Sweden, who has spent many years studying fertilization and early embryonic development in sea-urchin eggs.

SIX BLOOD-GROUP ANTIBODIES IN THE SERUM OF A TRANSFUSED PATIENT

BY

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The purpose of this note is to call attention to another instance of the formation of multiple blood-group antibodies after transfusion. The recipient was suffering from an undiagnosed collagen disease. The name "collagen disease" is conveniently used in the United States to denote a group of diseases, such as periarteritis nodosa and lupus erythematosus, which are of unknown aetiology but have certain common characteristics.

Sera containing multiple antibodies have twice before been reported. One of the donors was suffering from lupus erythematosus (Callender and Race, 1946) and the other from "osteosclerosis and extramedullary haematopoiesis" (Collins, Sanger, Allen, and Race, 1950).

Case History

The patient, a 30-year-old negro, was admitted to the Veterans Administration Hospital, Richmond, Va., on December 12, 1949, complaining of nausea, vomiting, and severe abdominal pain of about 12 days' duration. His illness began six years previously, and consisted then of migratory polyarthritis and serous pericarditis. A year later he was discharged from the Services, and at that time his skin and lips showed increased pigmentation. He had at one time suffered from exfoliative dermatitis subsequent to sulphonamide therapy. Ten months before admission he was in hospital for an undiagnosed condition which manifested itself by attacks of arthritis, angioneurotic oedema, endocrine dysfunctions, and gastro-intestinal irritability.

During the last few months he developed symmetrical, scaly, dry, pigmented lesions over the deltoid and infraclavicular regions.

It has not been possible to discover whether the patient was transfused during either of his stays in hospital: on neither occasion was he in a Richmond hospital.

Shortly after admission the patient was given three blood transfusions in one week (Table I) because of a severe hypochromic normocytic anaemia. Five days after the third transfusion he was noticed to be severely jaundiced, and his urine was blood-stained. Approximately six weeks

TABLE I.—*Transfusions of Patient*

No.	Date	Group of Donor	Reactions
1	Dec. 23, 1949	B, Rh+	
2	,, 28	B, Rh+	
3	,, 30	B, Rh+	
	Jan. 5, 1950		Severe haemolytic reaction
4	Feb. 28	B, cDe/cde, S−*	No reactions
5	March 8	B, cDe/cde, N, S−	
6	,, 24	B, cde/cde, S−	
7	,, 29	B, cDe/cde, N, S−	
8	May 10	B, cde/cde, N, S−	
9	,, 10	O, cde/cde, N, S−	
10	,, 18	O, cde/cde, N, S−	
11	,, 18	O, cde/cde, N, S−	

* The absence of S was presumed from the compatible cross-match; no other anti-S serum was then available in Virginia.

later it seemed advisable to transfuse the patient again, but by then it appeared impossible to cross-match him successfully. For this reason his blood was sent to one of us (R. K. W.). After identification of the various antibodies contained in the patient's serum he was transfused successfully several times.

Five months after admission he suffered the first of a series of three massive intestinal haemorrhages. From the first two he rallied, after transfusion, but during the third he died; this was about six and a half months after admission. Permission for a post-mortem examination could not be obtained.

During his stay in hospital the white cell count had varied from a leukaemoid level down to 2,000 per c.mm. At no time were "lupus erythematosus inclusion bodies" found in the polymorphonuclear leucocytes.

Summary of Serological Findings

The patient belonged to group B, N, cDe/cde or cDe/cDe (Table II). Anti-M was the first antibody to be identified

TABLE II.—*The Blood Groups of the Patient's Red Cells and the Antibodies in His Serum*

Patient's Groups	Antibodies in Serum
B	Anti-A
N, presumably S—	Anti-M and anti-S
cDe/cde or cDe/cDe	Anti-C and anti-E
Presumably Fy(a—)	Anti-Fy^a

in his serum; it was clearly shown by tests in saline at 15° C. Thereafter tests were confined to N blood samples. Titrations in saline at 37° C. demonstrated the presence of anti-C. Because a sample of N S cde/cde blood was agglutinated the presence in the serum of anti-S was suspected; it was subsequently proved by tests on O, cde/cde, N cells with and without the antigen S. The presence of anti-A could easily be demonstrated by an immediate reaction with A cells on a tile.

A strongly positive reaction with cDE/cDE cells suggested the presence of anti-E. This was proved by tests on saline suspensions of cells lacking A, M, S, and C antigens, but some with and some without the antigen E. Those with E were agglutinated, those without were not.

The shortage of available cells lacking the antigens A, M, S, C, and E made absorption necessary for the next stage. The serum was absorbed with blood A, B, MN S, P+, CDe/CDe, Lu(a−), K−, Le(a−), Fy(a−), and, as this did not of course remove the anti-E, further tests were confined to blood samples lacking E. Indirect antiglobulin tests then disclosed the presence of anti-Fy^a. This example of anti-Fy^a, unlike others so far described, is capable of giving weak reactions with Fy(a+) cells suspended in saline.

The following antibodies were not present in the serum: anti-B, -O, -H, -N, -P, -D, -d, -c, -e, -Lu^a, -K, -k, -Le^b.

Once again it was rather disappointing that no "new" antibody could be found in the serum of a person obviously so apt to become immunized.

Comment

The possibility of a relationship between unusual ability to produce blood-group antibodies and certain diseases has been discussed in a previous paper (Collins *et al.*, 1950). No conclusions were reached, and the conjectures will not be repeated here.

The serum described in this paper, which is from a person suffering from an undiagnosed collagen disease, is the third most abundant in blood-group antibodies to be reported. The other two sera were from patients suffering from lupus erythematosus diffusus and from osteosclerosis with extramedullary haematopoiesis respectively. Recovery was straightforward.

Summary

A patient who suffered from an undiagnosed collagen disease and who had received many transfusions was found to have the following blood-group antibodies in his serum: anti-A, -M, -S, -C, -E, and anti-Fy^a.

We wish to thank Dr. J. Kriz, chief of the Laboratory Service, Veterans Administration Hospital, Richmond, Va., for his kind co-operation in obtaining the clinical data of this case. We also wish to thank Mrs. M. Waller for the initial serological work-up. We are grateful to Dr. B. H. Kirman, of the Fountain Hospital, Tooting, for his help in setting up the large panel of donors of test cells without which such an investigation as that here described is not possible.

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Medical Memoranda

Double-barrelled Enteric Intussusception Causing Volvulus

A number of unusual cases of intussusception were reported in the *British Medical Journal* of March 4, 1950 (page 525). Details of the following case may therefore be of interest.

Case Report

The patient, a girl aged 15, was admitted to hospital on February 25, 1950. In November, 1949, after an attack of influenza, she had suffered from aching central abdominal pain for one hour, which was considerably relieved by vomiting twice. Fourteen days later she had severe "gripping" central abdominal pain for two hours, also relieved by vomiting. On two further occasions, at six-weeks intervals, she had similar but more severe attacks lasting four to five hours and six to seven hours respectively. Fourteen weeks after the first sign of trouble and two and a half days before admission the sequence started again, but this time did not cease. She was referred to hospital, where she had been seen once as an out-patient with "intestinal colic." The possibility of mesenteric adenitis, Meckel's diverticulum, or recurrent intussusception was then suggested, but was difficult to prove.

On examination the girl was not unduly distressed or dry. Her pulse was 108, and respiration and temperature were normal. The abdomen was not rigid, but there was some tenderness and guarding in the subumbilical region and right iliac fossa. This area was filled with a diffuse soft swelling, in the centre of which was a firmer sausage-shaped mass 5–6 in. (12.5–15 cm.) long, running obliquely upwards to the right.

A provisional diagnosis of small-bowel obstruction probably due to intussusception was made, but it was felt that there was something unusual about it and that this was probably not the whole story.

A right subumbilical paramedian incision was made, revealing the presence of sero-sanguineous exudate. A number of coils of dilated small gut were found "bunched" together in the pelvic brim region, which on further exploration proved to be a volvulus of ileum in a clockwise direction. On untwisting this the centre of the affected gut proved to be an entero-enteric intussusception, which seemed much more bulky and solid than would be expected, and which had a very tight neck, with foul purulent fluid exuding from beneath it when any endeavour was made to open it up. Attempted reduction by milking was unsuccessful. The

mass was therefore resected and end-to-end anastomosis carried out, and the abdomen was closed without drainage.

The excised specimen was opened along the intussuscipiens and the thick dark-red congested intussusceptum was seen. This had a very narrow apex, which when slit up with scissors presented, rather unexpectedly, the apex of another intussusceptum, dark blue-black in colour. On incising this the entering layer was found to be yellow and necrotic. The neck of the outer intussusception just covered that of the inner, and both were very tight. The cause of the original invagination was found to be a polyp of moderate dimensions.

It seemed that the polyp had caused an intussusception, to the limits of the mesenteric attachment, and the ensheathing layer had contracted both at the neck and at the apex; this spasm and constriction formed the apex and was the cause of the second intussusception. The total mass was very bulky and solid, and the weight of this in an active gut combined to provoke the volvulus.

I wish to thank Mr. J. E. Stanley Lee for permission to publish this report.

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Meningitis Due to Leptospira Canicola

Since *Leptospira canicola* was first isolated in 1931 by Klarenbeek and Schüffner (1933) from the urine of a dog, and the first cases of human infection were recorded by Dhont *et al.* (1934), more than 150 cases have been reported (Alston, 1949). The first case in this country was recorded by Baber and Stuart (1946), and a number of cases have been reported since, several being of meningitic type and one only being fatal (Weetch *et al.*, 1949).

An article by Campbell *et al.* (1950) reporting six cases of canicola fever in Bristol, and the review of the subject in the same number of the *British Medical Journal*, have drawn attention to the subject. Signs of meningeal irritation are a not uncommon manifestation of the disease (Harvier *et al.*, 1946). The following case, which presented clinically as meningitis, is of interest, as infection with *L. canicola* was proved retrospectively in both the patient and her bull-terrier.

Case Report

A married woman aged 32 was admitted to hospital on August 29, 1949, complaining of headache, fever, and vomiting for six days. The headache had begun on August 23, and had grown steadily worse. She had been feverish and had vomited several times. There was no significant previous history.

The patient was acutely ill on admission, but was fully alert and co-operative. Her temperature was 100° F. (37.8° C.) and the tongue was coated. There was considerable stiffness of the neck and back; the abdominal reflexes were absent, but other reflexes were normal; there was no paralysis. No jaundice or conjunctival injection was noted at any time. A trace of albumin and a few epithelial cells were present in the urine, but no red cells or casts. Lumbar puncture produced a slightly turbid fluid, not under increased pressure. In view of the turbidity, treatment with sulphamerazine was begun while bacteriological results were awaited. The report on the cerebrospinal fluid was as follows: leucocytes, 585 per c.mm. (73% lymphocytes, 27% polymorphs); protein, 35 mg. per 100 ml.; sugar, 78 mg. per 100 ml.; chlorides, 760 mg. per 100 ml.; no organisms or acid-fast bacilli seen; sterile on culture.

The patient was admitted at a time when the incidence of poliomyelitis was high, and the clinical picture and cerebrospinal fluid findings would have fitted such a diagnosis, except that the cell count was considered to be rather high. The possibility of a choriomeningitis was considered, and blood samples were taken for agglutination tests, being repeated at intervals.

A second lumbar puncture on September 1 showed a fall of leucocytes to 310 per c.mm., with 86% lymphocytes. The Wassermann reaction of the fluid was negative. By this time the patient's condition had improved, and the meningeal signs were abating, though she was still pyrexial and had some headache. The total white cell count in the blood was 8,400, of which 53% were polymorphs.

Convalescence was uneventful apart from a transient rise of temperature on September 10 associated with a small thrombosis in the left calf. This prolonged her period of rest in bed. By September 30 there were no abnormal signs in the central nervous system, the neck stiffness having disappeared and the abdominal reflexes having returned. The cerebrospinal fluid on September 26 showed 13 leucocytes per c.mm., mainly lymphocytes; protein, 15 mg. per 100 ml.; sugar, 51 mg. per 100 ml.; and chlorides, 780 mg. per 100 ml.

Serological results were still not available when the patient was discharged on October 6, a tentative diagnosis of abortive poliomyelitis having been made. On October 11 Dr. J. C. Broom reported a positive leptospiral antibody titre, and another specimen of blood was taken. Further inquiries from the patient then revealed that her bull-terrier had suffered a rather vague illness with anorexia and abnormal passivity a few days after the patient's admission to hospital. The animal when examined (in the convalescent stage) by a veterinary surgeon showed clinical evidence of having had a leptospiral infection, and the dog's serum showed a positive antibody titre for *L. canicola*.

Antibody Titres Against Leptospira

		L. icterohaemorrhagiae	*L. canicola*
Patient	23/9/49 (32nd day)	Positive 1/1,000 Negative 1/3,000	Positive 1/3,000 Negative 1/10,000
Patient	19/10/49 (57th day)	Positive 1/100 Negative 1·300	Positive 1/3,000 Negative 1/10,000
Dog	12/11/49	Positive 1/30 Negative 1/100	Positive 1/1,000 Negative 1/3,000

In the first specimen of the patient's serum the titres against *L. canicola* and *L. icterohaemorrhagiae* were almost equal. This, I understand from Dr. Broom, is not an uncommon finding. By the time of the second test, however, the titres had characteristically diverged, to reveal *L. canicola* as the infecting organism. The titre of 1/1,000 against *L. canicola* which was found in the dog was a sufficiently high positive result to indicate a recent infection, and steps are being taken to ensure that the animal shall not remain a source of infection.

My thanks are due to Dr. D. MacIntyre for permission to publish this case, and to Dr. J. C. Broom and Dr. M. S. Ross for their help with pathological data.

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Reviews

BIOLOGICAL ASSAY

Biological Standardization. By J. H. Burn, D. J. Finney, and L. G. Goodwin. Second edition. Oxford Medical Publications. (Pp. 440. £1 15s.) London: Geoffrey Cumberlege (Oxford University Press). 1950.

Some idea of the rate at which the subject is growing in range, complexity, and practical importance is afforded by Professor Burn's decision to share the responsibility for what is essentially a second edition of his book with two other authors, each having expert knowledge of a particular aspect of its problems. Even the first edition, which appeared in 1937 in a German translation as well as in English, represented so big an advance on his relatively small book on *Methods of Biological Assay*, which had been published in 1928, that Professor Burn chose a fresh title for the new enterprise, with its more elaborate scale of treatment. And, indeed, the use of these quantitative methods in pharmacology, and of statistical methods for interpreting their results, has extended with a far greater rapidity than could have been predicted in those early days. It may even be suggested that this development of a truly scientific basis for the measurement of pharmacological and chemotherapeutic actions has been a necessary condition of the extraordinary advances which recent years have witnessed, and which are still in progress, in the medicinal treatment of diseases.

When Professor Burn began, in 1928, to make these methods of standardization available in detail to the growing circle of those using them, interest was largely centred on the setting up of national, based upon international, standards for certain remedies needing to be thus assayed, and on the requirements of the then new Therapeutic Substances Act. The work under review, while still attending to such needs, goes far beyond them. The major part of it, indeed, is now concerned with quantitative methods as used in research for the discovery and appraisement of new remedies, even though these, when their value has been established, are pure chemical substances requiring no routine biological control.

Dr. Finney's section on statistics, occupying about one third of the volume, and Mr. Goodwin's chapters on quantitative methods in research on chemotherapy both add greatly to the value of the book. But they increase the tendency to make it a handbook for the worker in pharmaco-therapeutic research, and thus to take it beyond the needs of those who seek guidance only for compliance with official requirements. To that extent the title *Biological Standardization* is ceasing to do justice to the value of the book in its present form, as Professor Burn himself recognizes in his preface. The title of its very modest predecessor, *Methods of Biological Assay*, would, in fact, be now more suitable. The book should in any case be widely in demand for industrial as well as academic researches, and is heartily to be recommended.

HENRY DALE.

VIRUS DISEASES

Virus and Rickettsial Diseases. By S. P. Bedson, M.D., F.R.C.P., F.R.S. A. W. Downie, D.Sc., M.D., F. O. MacCallum, B.Sc., M.D., and C. H. Stuart-Harris, M.D., F.R.C.P. (Pp. 383; 33 figures. 24s.) London: Edward Arnold. 1950.

This book will have a wide appeal. The enterprising student will find it simply written and free of the obscurities which tend to creep into writings on specialized subjects. The clinician will find both in the text and in a useful table at the end all he needs to know about the laboratory diagnosis of virus diseases and about methods of immunization against them. The epidemiologist, the laboratory worker, and others with a closer interest in the subject will be refreshed by an up-to-date and authoritative account of matters in which progress has been so rapid, and they will be interested in the authors' views on controversial questions. For the benefit of the still more searching inquirer the text is well documented, the references being to recent and more important papers. As the title almost demands, there is a clinical description of each disease, although much more space is given to the virus itself and the methods by which it can be recovered, maintained, and utilized.

Of the four authors, Bedson writes the three important introductory chapters on general aspects of the subject and that on the psittacosis–lymphogranuloma-venereum group. Downie discusses the pox diseases, herpes, measles, rubella, mumps, glandular fever, and bacteriophage, and Stuart-Harris influenza and other respiratory-tract diseases and rickettsial infections. What would appear to be the hardest, and certainly the most varied, task falls to MacCallum, since his subjects include several on which there is little to be said (warts, gastro-enteritis, and animal diseases uncommonly affecting man), one of which knowledge has advanced rapidly while this book was being printed (chemotherapy), and others, notably infections of the central nervous system, which are of such variety and, in some cases, obscurity that a concise account presents some difficulty. The two outstanding diseases in this group are fully described, but the paragraph on antirabic vaccination is unduly brief and inconclusive, and no mention is made of hyperimmune serum as an additional preventive. It might also have been mentioned that poliomyelitis virus vaccines have been used; that the results were disastrous, and the reasons for this, are matters of some interest.

There is a good account of epidemic hepatitis, with a careful analysis of the features in which it differs from homologous serum jaundice. Here some mention of the circumstances which enabled human volunteers to be used as guinea-pigs seems desirable. The illustrations are almost all photographic, showing viruses or tissue changes caused by them. The conventional diagram showing differences in virus-particle size is missing: some form of this and perhaps simple maps illustrating the geographical distribution of diseases when this is peculiar and noteworthy might be considered for the next edition.

L. P. GARROD.

SURGICAL DIAGNOSIS

Spezielle Chirurgische Diagnostik. By F. de Quervain. Edited by K. Lenggenhager. Tenth edition. (Pp. 767; 956 illustrations. M. 75.) Berlin: Springer. 1950.

This volume, to which, so far as I am aware, there exists no parallel, represents the life work of Fritz de Quervain. To those of us who knew and admired him every page is impressed by the direct simplicity of his character, his vast experience, and his penetrating insight into the essential background of any surgical problem. To have covered the whole field of surgery, with a grasp of detail that may often put the specialist to shame, is a unique achievement, for us no longer possible. Indeed, such an achievement as this was possible only to the head of a great Continental clinic with a devoted staff and unlimited clinical material at his disposal. And such a volume as this, quite beyond the capacity of any clinic in this country, makes one wonder whether our system of independence really produces the best work and whether we might not learn something from the team-work of the Continental clinic.

Being concerned solely with surgical diagnosis, the book naturally includes illustrations of every possible abnormality arising from development, injury, or disease. But it also includes illustrations, diagrams, and tables describing in detail every method in use for surgical diagnosis. For example, pyelograms are shown in profusion, and the radiographs of the biliary tract are very fine, while the discussion of diagnosis in these fields is excellent. Much space is given to the nervous system, both central and peripheral, and the description of lesions related to abnormalities and injuries of the spine is of special interest. I hope that an English edition will soon be produced, for I cannot imagine a surgeon working in any field to whom it would not be of value. And when it appears I hope that it will include a note on Fritz de Quervain, to whose lifelong effort we owe the book. The most unassuming of men, the little photograph of him at work on page 621 is typical of him. To those of us who knew him the book itself is full of memories of him, but others would like to know something of his life as a great surgeon and a great teacher.

HENRY SOUTTAR.

POPULATIONS IN THE FAR EAST

Public Health and Demography in the Far East. Report of a Survey Trip September 13 to December 13, 1948. By Marshall C. Balfour, Roger F. Evans, Frank W. Notestein, and Irene B. Taeuber. (Pp. 132; illustrated. No price.) New York: The Rockefeller Foundation (49, West 49th Street). 1950.

This interesting report is the work of a team of demographers and sociologists who undertook a survey trip financed by the Rockefeiler Foundation to review public health and population problems of human welfare in the Far East. It should be read by all who are interested in international problems of health. From September to December, 1948, members of the team visited Japan, China, Korea, Taiwan (Formosa), Indonesia, and the Philippine Islands. The authors have written excellent case histories of the population growth in each of the countries, and they develop the pattern of their discussion from the common and contrasting elements in the different histories. In most of the Far East people are densely settled on underdeveloped areas with relatively inadequate resources. Birth rates are resistant to change and high enough to increase populations even when death rates are very high. In these circumstances there is a danger that the processes of population change will function "like the governor of a machine, to keep the system in a static equilibrium of poverty and ill-health."

In the world to-day Far Eastern problems of human welfare are of outstanding importance, and they centre upon problems of population change. Of the various needs, the reduction of human fertility is at once the most important and the most difficult to attain. The background common to all the countries visited is the persistence of high birth rates, based on social customs developed throughout the centuries to safeguard the survival of society when mortality was unchecked, by ensuring maximum reproductive performance. These social customs involve family organization, marriage customs, the role of women, and religious and moral teaching which are all directed towards encouraging child-bearing. They are concerned with man's most intimate experiences and deepest beliefs and so may be changed only with great difficulty in the absence of a major social upheaval.

In the Western world there was sufficient room for expansion to permit the absorption of population while reproduction patterns were adjusted to a changing industrial society. In the Far East to-day there is no room for expansion left, and the only alternatives to population checks by famine and pestilence are the possibility of lowering reproduction rates even before industrialism has had time to influence effectively traditional ways of life. There is an urgent need not only for marriage at a later age, attained perhaps by emancipation of the woman, but for a cheap and effective contraceptive which could be used under primitive rural conditions. The development of such a contraceptive is not even in sight.

J. H. F. BROTHERSTON.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Sterilization in North Carolina. By M. Woodside. (Pp. 219. 20s.) London: Geoffrey Cumberlege. 1950.

Eternal Eve. By Harvey Graham. (Pp. 699. 42s.) London: William Heinemann. 1950.

Psychology and its Bearing on Education. By C. W. Valentine, M.A., D.Ph. (Pp. 674. 18s.) London: Methuen. 1950.

A Doctor in Siam. By J. M. May. (Pp. 224. 12s. 6d.) London: Jonathan Cape. 1951.

An Atlas of Human Anatomy. By B. J. Anson, Ph.D. (Pp. 518. 57s. 6d.) London: W. B. Saunders. 1950.

Cancer: Where We Stand. By S. Russ, C.B.E., D.Sc., F.Inst.P. (Pp. 192. 10s. 6d.) London: Geoffrey Cumberlege. 1950.

Biological Foundations of Health Education. Proceedings of the Eastern States Health Education Conference, April 1–2, 1948. (Pp. 169. 16s.) London: Geoffrey Cumberlege. 1950.

Clinical Electrocardiography. By F. F. Rosenbaum, M.D. (Pp. 200. 36s.) London: Geoffrey Cumberlege. 1950.

Non-Valvular Heart Disease. By H. A. Christian, A.M., M.D., LL.D., Sc.D., M.A.C.P., F.R.C.P.Can., D.S.M. (Pp. 71. 16s.) London: Geoffrey Cumberlege. 1950.

The Medical Works of Hippocrates. By J. Chadwick, M.A., and W. N. Mann, M.D., F.R.C.P. (Pp. 301. 20s.) Oxford: Blackwell Scientific Publications. 1950.

BRITISH MEDICAL JOURNAL

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BRITISH MEDICAL GUILD

The Conference of Local Medical Committees has decided that general practitioners in the National Health Service should be advised to withdraw from the Service if the claim for increased remuneration is not satisfactorily settled. If circumstances compel general practitioners as a whole to take such a grave step, then the British Medical Guild will have to organize and finance collective action. The British Medical Association, while it may formulate policy and advise that certain steps should be taken, cannot legally organize withdrawal from service. By its constitution it is unable to "support with its funds any object or endeavour to impose on or procure to be observed by its members or others any regulation, restriction, or condition which, if an object of the Association, would make it a trade union." The pros and cons of this position were set out at length in a report[1] by the Council two years ago, and commented on in a leading article[2] at the same time. It was found that, even if it could be done, there would be little if any advantage in converting the B.M.A. into a trade union, or in setting up a parallel trade union membership of which would be conditional upon membership of the B.M.A. Eminent lawyers were firm in their view that as medical men were neither workmen nor masters, and as medicine was not a trade, there would be no advantage in trade union status: for example, a medical trade union would not have the degree of legal immunity afforded by the Trade Disputes Act of 1906. What the B.M.A. has lacked is the power legally to *organize* collective opposition or to use money to this end. It can only *advise* opposition, although it seems clear from past history that the word advise has been interpreted with some freedom. To secure legally the necessary freedom the British Medical Association therefore advised that there should be set up a parallel body, closely linked with it, called the British Medical Guild, the trustees of which should be (and are) members of the Council of the B.M.A. The Guild can organize and finance collective action. It cannot form policy. It has no membership; although this appears anomalous, it ensures that there is no possibility of conflict with the B.M.A., and it also makes it possible for the Guild to assist any doctor whether a member of the B.M.A. or not. If the Guild had a membership then financial benefits could be extended to Guild members and to none other: this would exclude from benefit those members of the B.M.A. who had not in fact joined the Guild. The Guild's money comes from defence funds established by general practitioners, consultants and specialists, and medical officers in the public health service. The National Insurance Defence Trust has already contributed sums of money to the Guild Trust Fund. (The General Medical Services Committee will continue collecting money in the same way as did the N.I.D.T.) An appeal is shortly to be issued to consultants and specialists to contribute to a fund known as the Hospital Medical Staffs Defence Trust. An appeal has been issued to public health medical officers to contribute to a Public Health Service Trust. From these three separate trust funds money will be allocated to the Guild as the sectional trustees see fit. This arrangement is not very tidy. More effective expression of the unity of the profession might be given if these three funds were ultimately merged into one Guild fund.

Many practitioners appear to be uncertain what the Guild is, what its powers are, where its funds come from, and how they can support it. Apart from earlier descriptions of the Guild and its problems in this *Journal* there was in the *Supplement* of October 14, 1950, a statement in the form of question and answer which should make the position clear: the statement has been sent to every general practitioner in the National Health Service. But to make assurance doubly sure the trustees of the Guild are now issuing to local secretaries and group organizers a pamphlet which sets out the whole matter simply and effectively. There should now at least be little excuse for ignorance of what the Guild is and what are its objects.

The success of the Guild will depend upon the activity of the local Guild committees in the country. Honorary secretaries of B.M.A. Divisions have taken the initiative in setting these up, and it is hoped that the formation of "Guild groups" of eight to twelve practitioners (whether B.M.A. members or not) within each Division area will help to dissipate apathy and prepare the ground for collective action if such becomes necessary. If collective action is to be effective the grounds for it must be unambiguous; so far as

[1] *Supplement to British Medical Journal*, 1949, 1, 95.
[2] *British Medical Journal*, 1949, 1, 354.

is possible there must be convinced and unanimous agreement on the principal issues; and above all there must be really substantial funds at the disposal of the trustees of the Guild. It is true there is a general movement in these desired directions; but there is need for a quickening of interest and activity if the Guild is to get into fighting trim for a battle which may not be far away.

ABSORPTION OF IRON

The administration of iron salts is an essential part of the treatment of certain anaemias. Iron compounds differ very much in their value as therapeutic agents: ferrous salts are generally considered to be more efficacious than ferric salts, while complex organic compounds containing iron, such as haemoglobin, are of no value. Moore and his colleagues[1] found that the dog, unlike man, can absorb iron from ferric compounds as readily as it does from ferrous salts. To be effective large doses of iron must be given, but there has never been a satisfactory explanation for this. It has been claimed that the absorption of iron in man is aided by giving acid and impaired by alkali.[2 3] Hahn and his colleagues[4] and Granick[5] have put forward the modern view of the factors controlling iron absorption. Both have worked on laboratory animals; the former used radioactive tracers and the latter histochemical methods. They hold that iron is absorbed from the intestinal tract in response to a demand from the body for more iron: in the absence of this demand there is a "mucosal block" which prevents the absorption of iron. Granick believes that a substance called "ferritin" plays an important part in controlling iron absorption. Ferritin was isolated by Laufberger[6] in 1937 and is a readily crystallizable protein containing as much as 20% iron. An ill-defined protein material containing 7% of iron was isolated from pig's liver by Schmiedeberg[7] 40 years before and called by him "ferratin." The properties of ferritin have been reviewed by Michaelis.[8] It is formed by the addition of iron to a protein complex named "apoferritin," which has the same crystalline structure as ferritin, but the crystals are colourless while those of ferritin are brown. Apparently apoferritin is not normally present in the tissues but is formed only as a result of some stimulus provided by the presence of iron. Granick believes that apoferritin is being continuously formed and broken down in the intestinal wall, but that the breaking-down process is halted when the iron unites with the apoferritin. What happens next is obscure. There is no evidence that ferritin ever exists in the blood stream, but it can be isolated from the liver, spleen, kidney, and intestinal mucosa.

Nothing is known about the route taken by the iron as it travels between the intestine and the tissues where it is used. A globulin fraction in human plasma contains iron,[9 10] and it is believed that when there is a demand for new iron the tissues take it first from the plasma, and this is then replenished by absorption from the gut. It is perhaps worth pointing out that if ferritin itself was absorbed from the intestine it would travel via the lymphatics rather than via the blood stream because of its considerable molecular size. Such a path of absorption was described by Quincke[11] in 1890, when he was studying iron absorption in animals given iron salts in their diet. It is also the path followed by the iron-containing pigment that is deposited in the duodenal mucosa after the injection of tannic acid.[12] There are, however, other important factors that control the absorption of iron, and these have been ignored by the proponents of the "mucosal-block" theory. Kinney and his colleagues[13] have recently reported that rats fed on a diet of corn grits to which is added 2% ferric citrate show large deposits of iron in the hepatic cells, especially those at the periphery of the lobules. They found that this effect was related to the low phosphate content of the grits diet, and could be prevented by adding phosphate to the food. There is good chemical evidence in support of the belief that phosphate ions might prevent the absorption of iron. Ferric phosphate is totally insoluble, even below *p*H 5, and ferrous phosphate becomes soluble only on the acid side of neutrality. The interference by phosphate is generally accepted by authorities on mineral metabolism.[14] This fact does not seem to be appreciated by those who administer iron to patients, and some of the experimental work bearing on this point is worth describing.

Happ[15] studied the anaemia that developed in certain groups of rats that were on rachitogenic diets. Rickets could be produced by a diet containing either a high proportion of phosphate and a low proportion

[1] *J. clin. Invest.*, 1944, **23**, 755.
[2] Kellogg, F., and Mettier, S. R., *Arch. intern. Med.*, 1936, **58**, 278.
[3] Mettier, S. R., and Minot, G. R., *Amer. J. med. Sci.*, 1931, **181**, 25.
[4] *J. exp. Med.*, 1943, **78**, 169.
[5] *J. biol. Chem.*, 1946, **164**, 737; *Science*, 1946, **103**, 107.
[6] *Bull. Soc. chim. biol.*, 1937, **19**, 1575.
[7] *Pharmakologie*, 1902, Leipzig, p. 432.
[8] *Advances in Protein Chemistry*, 1947, **3**, 53.
[9] Schade, A. L., and Caroline, L., *Science*, 1946, **104**, 340.
[10] Rath, C. E., and Finch, C. A., *J. clin. Invest.*, 1949, **28**, 79.
[11] *Z. allg. Path.*, 1896, **7**, 389.
[12] Barnes, J. M., *Brit. J. exp. Path.*, 1948, **29**, 495.
[13] *J. exp. Med.*, 1949, **90**, 137.
[14] McCance, R. A., and Widdowson, E. M., *Ann. Rev. Biochem.*, 1944, **13**, 322.
[15] *Bull. Johns Hopk. Hosp.*, 1922, **33**, 163.

of calcium or a high proportion of calcium and a low proportion of phosphate. In those animals fed a high phosphate diet anaemia developed in addition to the rickets.

Cox and his colleagues[16] reduced the ash content of guinea-pigs' bones by giving them an excess of iron in the diet. Brock and Diamond[17] fed rats with large doses of iron and observed in them rickets of the same severity as that seen after feeding a low-phosphorus (Stienbock) rachitogenic diet. They reported that there were no histological abnormalities in the tissues other than bone, but presumably no special search for iron was made. Deobald and Elvehjem[18] produced rickets in chicks by the same means. In other words, iron can behave like beryllium and aluminium and cause rickets in animals by preventing the absorption of normal amounts of phosphate from the diet. Elvehjem and his colleagues[19] studied the natural "anaemia" of infants and raised the amount of haemoglobin in the blood by feeding ferric pyrophosphate, but they warned against the administration of iron in too great a quantity in case the infant might thereby be deprived of phosphate and develop rickets. It is rather surprising to read in a later paper with Elvehjem as a co-author[20] the conjecture that "from a strictly chemical point of view there is no reason to suspect that high levels of phosphate (in the diet) should prevent iron assimilation." These workers went on to show that the anaemia of milk-fed rats given iron responded best when the diet had a Ca : P ratio of 0.45, but with larger amounts of calcium the response was not so good. They conclude: "Our results, together with those of other workers reviewed here, seem to indicate that within limits ordinarily reached in most diets, calcium impedes the absorption of iron, while phosphorus has the opposite effect." However, an examination of the papers to which they refer shows that, in fact, the balance of the evidence would appear to support exactly the opposite conclusion. Day and Stein[21] measured the rate of recovery of anaemia in rats given diets containing varying amounts of phosphate, iron, calcium, and other salts. They found that recovery was slowest when the phosphate content of the diet was high, but this effect could be neutralized by feeding beryllium carbonate. Calcium also improved the rate of recovery if given as the carbonate, but not if given as the phosphate. They concluded that a high-phosphate content of the diet will impede the absorption of iron, and that calcium stimulates iron absorption only indirectly by removing phosphate.

None of the papers just referred to are accompanied by histological evidence of iron absorption, whereas the work of Kinney and his colleagues on the grits diet points to the conclusion that the absorption of iron in gross excess leads to a heavy deposit of iron within the hepatic cells. Similar deposits of iron have been observed in rats fed a normal diet containing 2% ferric citrate to which had been added 2% beryllium carbonate to lower the free-phosphate content of the diet. The deposit does not occur if either iron or beryllium salts are given alone. Taylor and his colleagues[22 23] have seen exactly the same changes in cats after the removal of the pancreas or tying the pancreatic duct. They claimed to have found atrophic changes in the epithelial cells lining the gut, which they thought led to an increase in the cells' permeability to iron salts, and they suggested that such changes might be the result of a deficiency of vitamin A. Gillman and Gillman[24] described exactly the same type of iron deposit in the liver cells of African natives suffering from pellagra. They thought that the iron became deposited around the mitochondria of the liver cells because their function was disturbed by the general nutritional deficiencies associated with the pellagra. In a later paper[25] they reported confirmation of the observations of Taylor and his colleagues on the effect of tying the pancreatic duct in cats. They showed that the increased deposit of iron in the liver was not affected by giving vitamin A.

It is clear, therefore, that a low-phosphate content of the diet, the absence of the external secretion of the pancreas, and a general nutritional disturbance (pellagra) will produce exactly the same picture of an excessive deposit of iron in the livers of rats, cats, and man. These findings make it clear that a "mucosal block" controlled by the need of the body for iron is not the only factor that determines the amount of iron that is to be absorbed from the alimentary tract. Although the part played by the presence of phosphate in preventing the absorption of iron has been well recognized in the experimental field, its possible importance in clinical practice does not seem to have been appreciated. It is not mentioned in standard textbooks on therapeutics. Of a more limited clinical interest is the fact that in the absence of a normal amount of free phosphate in the diet an excessive amount of iron may be absorbed and deposited in the liver and spleen, as in haemochromatosis.

[16] *J. biol. Chem.*, 1931, **92**, Proc. XI.
[17] *J. Pediat.*, 1934, **4**, 442.
[18] *Amer. J. Physiol.*, 1935, **111**, 118.
[19] *Amer. J. Dis. Child.*, 1935, **50**, 28.
[20] *J. Lab. clin. Med.*, 1940, **25**, 464.
[21] *J. Nutrit.*, 1938, **16**, 525.
[22] *J. Path. Bact.*, 1931, **34**, 793.
[23] Ibid., 1935, **41**, 397.
[24] *Arch. Path.*, 1945, **40**, 239.
[25] *Nature, Lond.*, 1947, **159**, 875.

EPIDEMIOLOGY OF INFANTILE ENTERITIS

Much may be learned about the epidemiology of an infection without precise knowledge of the causative agent, but rational methods of prevention and control may not be applicable without this knowledge. For instance, the danger of infantile enteritis, still one of the most important causes of death in infancy, could be enormously reduced by a single measure—breast-feeding of all infants for 6 to 9 months—but its universal application is impracticable. In the meantime a knowledge of the causative agent or agents and their mode of spread would help in planning more rational control measures. This was the theme of a recent discussion opened by Dr. Joan Taylor and Dr. K. B. Rogers at the Epidemiology Section of the Royal Society of Medicine. Dr. Taylor prefaced her review of aetiological and epidemiological factors by defining the entity as an "infective infantile enteritis." It should include all primary infective gastro-enteritis from birth to one year; not that the first birthday is a barrier, but the infection, if it occurs, is rarely serious after this age. Dietetic upsets and parenteral gastro-enteritis associated with primary disease elsewhere, like respiratory and urinary infections, should be excluded. Dr. Taylor commented on the difference in emphasis on the age incidence here and in the U.S.A.: institutional midwifery is the rule there and neonatal diarrhoea a serious problem, whereas in Britain outbreaks among "deprived" children in residential nurseries are more common.

Some years ago a form of gastro-enteritis, more common in winter than in summer, which affected both adults and young children, was prevalent in many maternity departments in this country. A similar syndrome was noted in the U.S.A., and there the evidence incriminating a virus was strong, since human volunteers were infected both by inhalation and ingestion of faecal filtrates. Recently Keitel[1] has found cold agglutinins and agglutinins to the non-haemolytic streptococcus MG in the blood of over 50% of affected infants and young children (serological reactions similar to those seen in cases of primary atypical pneumonia). The work of Light and Hodes[2] on the experimental infection of calves with a filterable agent from the stools of infants with neonatal diarrhoea, unassociated with adult infection, indicated that a virus was also the cause of this syndrome, though the natural susceptibility of calves to scours justified a note of caution. Among those investigating possible bacterial causes of epidemic enteritis, Bray,[3] in this country, was the first to draw attention to a lactose-fermenting serologically specific type of *Bact. coli*. His findings were corroborated by Giles and Sangster,[4] who found the same serological *Bact. coli* associated with a widespread outbreak in Aberdeen in the summer of 1947, and since then this organism and another lactose-fermenter, also first isolated in Aberdeen and called by Smith[5] the β type, have been incriminated in many outbreaks of gastro-enteritis in Scandinavia and the U.S.A., as well as in Britain.

Evidence for a causal relationship between one or other of these *Bact. coli* strains and infectious enteritis in infants includes its presence in large numbers in the faeces immediately before and during the acute illness and its disappearance in convalescence; the occurrence of infection in a residential nursery soon after its introduction; the association with infantile enteritis of these specific serological types of *Bact. coli* in many different parts of the world; and their apparent absence from the stools of healthy infants who have had no contact with those suffering from the disease. To this may be added the development of enteritis in adult human volunteers who drank cultures of *Bact. coli* α type.[6] Puzzling features are the long incubation period, up to 7–10 days, when the organism may be demonstrated in large numbers in the stools; the virtual absence of acute inflammatory reaction in the bowel in contrast to the findings in salmonella and shigella infections; and the apparent lack of antibody response. Another odd finding mentioned by Dr. J. E. Jameson at the R.S.M. meeting was a tendency for the organism to lose virulence after some months' persistence in an institution; Payne and Cook[7] noted its spread in a residential nursery without serious clinical infection. Most of the positive findings have occurred in outbreaks of gastro-enteritis, and it is still uncertain what association there may be between these specific *Bact. coli* strains and the apparently sporadic infection of infants in their own homes; a majority of the infants admitted to hospital for the treatment of the disease are in this group.

Rogers described the spread of infection within the wards of a modern hospital and the spread from one hospital to another of gastro-enteritis in which the α and β types of *Bact. coli* apparently played a part. He thought that the ease with which these organisms could grossly contaminate the environment was related to the large numbers excreted and their dissemination from the napkins in a manner akin to the dispersion of organisms from the discharges of a burn. They were present on blankets and cots, dust, floors and walls, baths and wash-basins, on ointments, in the drawers of bedside lockers, and on the hands of nurses even after scrubbing-up. Means of easy passage from one cubicle to another were the communal broom and the pram used for the transport of infants. About one-third of the infants acquired these potentially dangerous organisms after admission, and about one-fifth of all those admitted became seriously ill from this cross-infection. Gastro-enteritis was also responsible for 60% of the increased stay in hospital among infants with pyloric stenosis who developed some complication necessitating additional treatment. It seemed possible that vomiting babies in out-patient departments might set in train a series of outbreaks in different hospitals. There was also some evidence of spread of infection in the home from indirect contact: the specific *Bact. coli* can persist in dust for as long as 17 days. Rogers did not find chloramphenicol effective as a prophylactic measure, and he recommended the use of a vacuum cleaner and the oiling of floors to reduce the spread of infection by contaminated dust.

[1] *J. Infect. Dis.*, 1950, **86**, 219.
[2] *J. exp. Med.*, 1949, **90**, 113.
[3] *J. Path. Bact.*, 1945, **57**, 239.
[4] *J. Hyg., Camb.*, 1948, **46**, 1.
[5] Ibid., 1949, **47**, 221.
[6] Kirby, A. C., Hall, E. G., and Coackley, W., *Lancet*, 1950, **2**, 201.
[7] *British Medical Journal*, 1950, **2**, 192.

TREATMENT OF THE SHORT LEG

The treatment of legs of unequal length illustrates well the concern of orthopaedics not only with disabilities of structure and function but also with their associated psychological effects. With modern treatment distressing inequalities are not so often seen as they used to be. Apparent inequality, the result of pelvic tilt in hip disease, is readily correctable by the stabilizing operation usually necessary. Actual shortening of the same origin, if not more than an inch or so, can be compensated by fixing the affected hip in slight abduction. The causes of shortening giving rise to the greatest anxiety are those due to various forms of aplasia or dysplasia; these include such conditions as epiphysial arrest at the knee due to prolonged immobilization of a tuberculous hip; the inhibition of growth in a leg after poliomyelitis; and congenital hemiatrophy. For these the provision of a raised shoe is, for the individual affected, not always a satisfactory solution. The best treatment for really severe shortening of 5 inches (12.5 cm.) or more may be the provision of an extension prosthesis, though for some patients amputation and an artificial limb are preferable. Surgical methods (if reliable and safe) should be considered for the intermediate inequalities of 1½ to 5 inches (3.8–12.5 cm.). Elsewhere in this issue two surgeons discuss such methods from opposite viewpoints. Mr. A. L. Eyre-Brook states the case for shortening the normal long leg and Mr. F. G. Allan that for lengthening the affected limb. The former rightly puts emphasis on bone-shortening when growth is finished, but he also gives a valuable account of an improved technique for arresting epiphysial growth in childhood by Phemister's operation. In the U.S.A. Blount has introduced a method of retarding growth mechanically by inserting staples which overlap the metaphysis and epiphysial cartilage above and below the knee. With this method there appears to be less risk of undesirable complications (such as disorders of growth) than with the earlier methods of epiphysiodesis. Theoretically it is better to lengthen a short leg than shorten a normal one, and the results obtained by Allan in a series of 101 cases are impressive. In his experience the hazards of this method of treatment can be controlled.

During the discussion which followed the reading of these two papers at the Annual Meeting of the B.M.A. in Liverpool last summer, Mr. H. J. Seddon emphasized that these operations, particularly as they apply to limb lengthening and to operations upon the normal epiphyses of children, should be performed only in special centres by surgeons prepared to master the complicated techniques required.[1] The patient's mental reaction must not be forgotten: for a condition requiring treatment largely because of cosmetic and therefore psychological need, surgeons should consider whether they are justified in condemning a child to a diminution of stature by shortening his normal limb at a time when he has no power of decision for himself. If for no other reason Eyre-Brook is wise to point out the advantages of bone-shortening by some form of overlapping osteotomy when growth is finished. Obviously the ideal solution has not been found. What is needed—apart from the prevention of inhibited bone growth—is a physiological method of stimulating it. Harris[2] attempted this in cases of poliomyelitis by performing lumbar sympathetic ganglionectomy, but the small amount of improvement obtained (about one inch) meant that the operation was not of much use for the patients most in need of treatment. Further, it had to be done before the age of 6 in order to obtain the best results.[3]

1 *British Medical Journal*, 1950, **2**, 358.
2 *J. Bone Jt Surg.*, 1930, **12**, 859.
3 Harris, R. I., and McDonald, J. L., ibid., 1936, **18**, 35.

I.A.T.A. MEDICAL COMMITTEE

The International Air Transport Association (I.A.T.A.), which is composed of 68 of the main airlines of the world and looks after the interests of commercial aviation to achieve the maximum economy, efficiency, and safety in passenger flying, was established in Havana in April, 1945. Three years later the association felt the need for medical advice and therefore formed a small medical panel. Last year, however, the executive committee raised the status of the panel to that of a standing committee, in recognition of the growing importance of the medical aspects of international air transport. As a result the work of airline medical officers will now be better co-ordinated on a world-wide basis with other I.A.T.A. activities for the benefit of both aircrew and passengers.

The importance of the newly created I.A.T.A. medical committee, whose membership is limited to 18, can be judged by its terms of reference and the agenda of the first meeting, due to be held in Cairo on February 5–9 1951. This meeting-place is particularly suitable, since Egypt is specially interested in quarantine regulations to prevent cholera being introduced from the East, particularly from India, and against the spread of yellow fever from Central and West Africa. The terms of reference of the committee are that it shall concern itself with the physiological, psychological, hygienic, and general medical aspects of all matters affecting the safety and efficiency of aircrew and passengers in flight and at airports. The agenda for the first meeting, which will be attended by Sir Harold Whittingham, the director of medical services of B.O.A.C., and Dr. A. B. Barbour, chief medical officer of B.E.A., includes aircrew fatigue and flight-time limitations; the carriage of sick passengers; the hygiene of airports; review of the draft International Sanitary Regulations of the World Health Organization so far as they concern aviation; review of the International Commercial Aviation Organization's (I.C.A.O.) medical requirements for aircrew in the light of experience; standardization of oxygen regulations for international air travel; recommendations for maintaining wholesome water supplies on aircraft; medical arrangements for crashes and first-aid at airports; minimum requirements for aircraft first-aid kits, including the need or otherwise to provide morphine; and physiological

requirements in the event of sudden decompression at high altitudes. Most of the members of the committee have practised aviation medicine for many years. Their work promises to be of great value, for they can advance recommendations based on practical experience, and so help to ensure that the human factor is taken into account in any mandatory requirements on commercial aviation issued by I.C.A.O., W.H.O., or any Government.

AORTIC STENOSIS

The account of the symptoms and physical signs of aortic stenosis by Dr. D. Lewes published elsewhere in this issue of the *Journal* confirms that the conception of the clinical features of this disease has changed considerably in recent years.[1] It was once a cardiological dogma that aortic stenosis should be diagnosed only in the presence of a palpable thrill, enlargement of the left ventricle, a systolic bruit, and a slow-rising pulse.[2] More recent studies have shown that adherence to these strict criteria has been responsible for a failure to diagnose aortic stenosis in the majority of cases. In 1948 Kumpe and Bean[3] correlated the clinical and necropsy findings in 107 cases of pure aortic stenosis; they showed that the classical physical signs were present only in about one-fifth of their cases and suggested that a diagnosis of aortic stenosis should be considered in the presence of a loud precordial systolic murmur and an alteration of the aortic second sound. In addition they pointed out that a number of symptoms—such as post-exertional cardiac pain, attacks of sweating, syncope, vertigo, and mental confusion—were commonly found in patients with aortic stenosis. These findings were later confirmed by Davies and Steiner in a smaller series of cases.[4] Lewes again draws attention to many of the features described by previous authors—for example, the high incidence of aortic stenosis in men and its occurrence in the older age groups. In particular he clearly describes a number of symptoms which are becoming recognized as being characteristic of aortic stenosis: the most common are dyspnoea, cardiac pain, attacks of pallor, sweating, and giddiness, and other manifestations of cerebral anoxia. An unexpected finding was that four of Lewes's 25 patients died from bacterial endocarditis. This complication is not usually regarded as being common in the elderly.

It is evident that aortic stenosis has been underdiagnosed in the past. The finding of a harsh systolic murmur over the praecordium, whether localized to the aortic base or not, must be regarded as strong evidence of aortic stenosis, especially when found in the middle-aged or elderly patient. Radiology provides the most useful confirmation of the diagnosis, since calcification of the aortic valves can almost always be demonstrated either by fluoroscopy or tomography.[4]

1 *British Medical Journal*, 1950, 1, 1126.
2 Lewis, T., *Diseases of the Heart*, 1940, London.
3 *Medicine, Baltimore*, 1948, 27, 139.
4 *Brit. Heart J.*, 1949, 11, 126.

QUACKERY IN NORWAY

The Norwegian anti-quackery law of 1936 forbids the treatment of epidemic and infectious diseases, tuberculosis, venereal disease (even if it is not in an infectious stage), cancer, diabetes, and dangerous forms of anaemia and goitre by persons not holding the official *licentia practicandi*. The public, it was hoped, would be effectively protected by this law from at any rate the most dangerous manifestations of quackery. But recent events outside and inside the Norwegian Storting, or Parliament, suggest that the public's interest in such protection is languid and in some quarters actively hostile. Two faith healers from the U.S.A. recently conducted mass meetings in Norway at which healing by faith was dramatically demonstrated. One reaction to these meetings was a call for the immediate tightening-up of quack legislation. Another reaction was an outburst against the monopoly of healing by duly qualified practitioners. These and other reactions led last summer to a full-dress debate in the Storting, where orthodox medicine was attacked from more than one side, including that of the intelligentsia. The president of the Storting, Herr Hambro, argued that if the present anti-quackery law is to be revised attention must be paid to faulty treatment by experts as well as to such treatment by the inexpert. The treatment meted out to patients by doctors was, he implied, often sheer quackery, and he warned the Storting against too much intervention by legislation on behalf of the temporal convictions of a certain class or profession. Another speaker deplored the attitude of omniscience of young doctors in particular. Just as some legislators, when confronted with prohibition, would rather their country was free than forced to be sober, so on this occasion many speakers wanted freedom in connexion with their own health. Every thoughtful student of this debate must have been struck by the great interest taken by the country's legislators in prayer as a means to heal the sick, and by the fear of allowing a single class or profession to monopolize the art of healing. At present only qualified doctors can draw payment for medical treatment from the national sickness insurance funds. Nature healers and faith healers may not do so even in the case of the relatively harmless diseases not mentioned in the law of 1936. A movement is now on foot to do away with this discrimination. But if and when a nature healer or faith healer is promoted in this sense his even less orthodox competitors will surely feel the time has come to press their claims.

The next session of the General Medical Council will open on Tuesday, February 27, at 2 p.m., when the President, Professor David Campbell, will take the chair.

We record with regret the death of Dr. O. H. Mavor on January 29 in Edinburgh. Dr. Mavor, who, as James Bridie, achieved international fame as a dramatist, was 63 years of age.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

CHRONIC SUPPURATION IN THE MIDDLE EAR

BY

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The term "chronic suppuration in the middle ear" may be applied to any inflammation of the middle ear which has given rise to a perforation of the drumhead, shows no tendency to heal, and is associated (with some important exceptions) with a more or less continuous discharge of pus. No fixed period of time can be laid down, but any discharge which shows no signs of clearing in five to eight weeks is usually regarded as chronic by most otologists.

Probably all such cases date from one or more attacks of acute inflammation, and even those which appear insidiously are likely to have arisen from forgotten or overlooked acute otitis media in infancy. About one case in five is directly attributable to the infectious diseases of childhood. Forster has stated that in taking case histories of children with chronic suppuration he has frequently found a hereditary tendency.

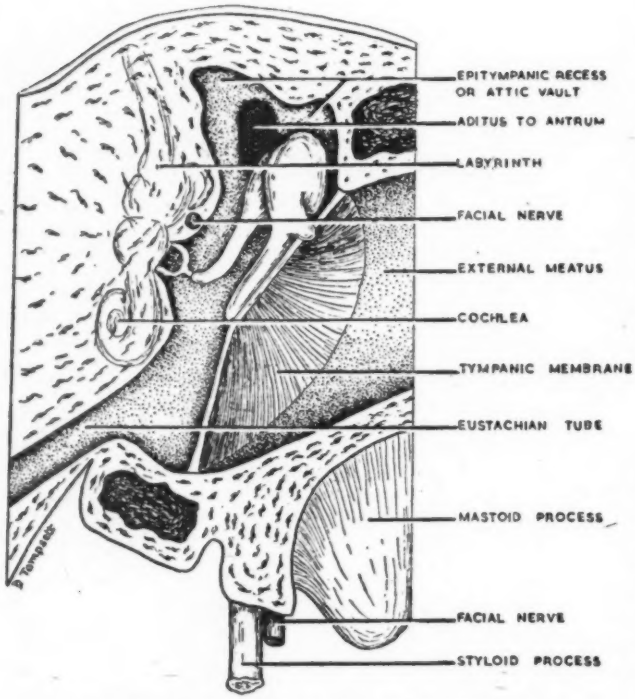

FIG. 1.—Diagrammatic section of left middle ear.

Patients with cleft palates whose widely open nasopharynges are particularly prone to infection often suffer from an associated chronic suppuration of the middle ear.

Pathology

Turmarkin has pointed out that the middle-ear cleft is lined by ciliated epithelium in its tympanic or lower part and by squamous epithelium in the attic vault or upper region (Fig. 1). The two areas might therefore be expected to respond differently to acute infection.

In the tympanic area an acute infection may resolve rapidly and completely with or without treatment. If, however, perforation occurs, this is usually central and does not involve the surrounding bone; through the perforation a persistent mucopurulent discharge may develop.

In the attic vault acute infection may lead to rapid perforation through or behind Shrapnell's membrane, sometimes with necrosis of adjacent bone; alternatively, there may be epithelial desquamation and the collection of debris.

Cholesteatosis

If debris collects it may cause a slow perforation, usually associated with necrosis of bone, although occasionally the condition may subside and remain quiescent until another attack. These masses of debris give rise to the condition formerly known as cholesteatoma but which is now better described as cholesteatosis. Once formed the masses become quite big, and it is these cases which are the main exceptions to the definition given in the opening paragraph. The masses consist of epithelial cells, pus cells, organisms, and cholesterol; even when not actively infected they can erode neighbouring bony structures and may cause destruction of ossicles or, occasionally, exposure of the dura mater of the middle or posterior fossa and lateral sinus.

Reservoirs of Infection

It is important to remember that infection usually reaches the middle ear via the Eustachian tube, and the persistence of infection at the pharyngeal end of the tube may account for a chronic aural discharge. Also, a cellular mastoid may be infected at the time of the primary acute otitis and, while not going on to an acute mastoiditis, may remain a reservoir of infection constantly overflowing into the middle ear. In such cases the discharge may be minimal when the patient is recumbent but may become profuse when he raises his head—for example, on getting up in the morning.

The predominating organism is probably that which caused the original infection, but it may be any one of the many organisms which cause acute nasopharyngeal inflammation. Some form of streptococcus is probably the commonest, but in chronic cases the infection has invariably become a mixed one and is commonly resistant to chemotherapy or treatment with antibiotics, either local or systemic.

Clinical Course

The changes in the mucous membrane may vary from simple hyperaemia to complete destruction. In the simplest form the swollen mucosa, with epithelium intact, may encroach considerably on the cavity of the antrum, and in such a case the decongestive action of ephedrine (1%) combined with silver proteinate (10%) and spirit (10%) in water may be very beneficial. In

the severer forms the epithelial covering is lost over considerable areas, with the formation of granulations and, if these become organized, adhesions or fibrous masses. However, where there is underlying necrosis of bone, organization of the granulation tissue rarely takes place. Sometimes polypoid masses consisting of granulation tissue form, and these may become partially organized and covered by epithelium.

Where resolution of the infection after destruction of the mucosa has been complete, areas of bare shiny bone may be seen through large inferior perforations and the remains of denuded ossicles may stand out clearly (Fig. 3, H).

In cholesteatosis bone may be eroded without the usual signs of suppuration, the enlarging cavity retaining everywhere a well-defined epidermal covering. In such cases there may be little or no demonstrable discharge. In other cases suppurative necrosis coexists or alternates with absorption of bone, and the pus may be so offensive as to form a social barrier between the patient and his fellows. In acute otitis media and chronic tubo-tympanic infections the pus is rarely offensive.

Now and again the erosion of cholesteatosis opens the whole vault, aditus, and antrum into the meatus, and nature is found to have performed a perfect radical mastoid operation. Occasionally a track will be formed under the integuments of the roof or posterior wall of the meatus, and a cholesteatotic mass will present far from its origin as a swelling; this is often mistaken for a furuncle. If the swelling is incised, foul-smelling material is discovered and bare bone can usually be felt.

Multiple perforations are said to be characteristic of tuberculous infection, and the tubercle bacillus may be found in the pus.

Signs and Symptoms

Apart from discharge from the ear and impairment of hearing, a large proportion of patients endure chronic suppuration of the middle ear for years without pronounced disturbance, either general or local. In fact many of those whose hearing is still good are unaware that anything is or ever has been wrong with their ears This was clearly demonstrated in the examination of recruits for National Service: routine otoscopy revealed long-standing and often advanced chronic suppuration of which the candidates appeared quite genuinely unaware. While it might be thought that constant purulent discharge would be accompanied by systemic disturbance, it is a clinical fact that such is absent in most cases. Constitutional changes, such as fever and a raised pulse rate, should suggest the possibility of intracranial complication; rigors, the onset of facial paralysis, vertigo and vomiting, and neck rigidity are all of serious import.

Sometimes headache, which may be hemicranial in character and located particularly over the homolateral temporal region, is complained of; often this is not associated in the patient's mind with something wrong with his ear. When present it invariably indicates bone necrosis and may mean exposed dura mater. It is a strong indication for surgical exploration.

An acute flare-up of an old infection is always a dangerous situation, and when signs of acute mastoiditis develop immediate operation is indicated. It should be remembered that in old people with mastoiditis fever is often absent, and that in these subjects headache, local tenderness, and constitutional disturbance are sufficient to warrant exploration.

The characteristics of the discharge have already been mentioned. Quiescent attic disease may easily escape notice on account of the formation of a scab or crust over the perforation and neighbouring meatal wall, which, because of its brown colour, is often mistaken for wax. All debris and crusting should be softened and removed by syringe or gentle mopping with a wool-headed probe before a meatus and drumhead are passed as normal.

Hearing

When the lesion is in the tympanic area hearing is impaired in almost every case, the loss being due to the partial or complete destruction of the membrana tensa, with consequent immobilization of the malleus and incus, or to hyperplastic changes in the fossa ovalis interfering with the mobility of the stapes. In those cases in which the membrana tensa has been largely destroyed appreciation of low frequencies is lost; high notes are often well heard. Yet it is surprising how well some patients with almost total loss of the drumhead, and even of the malleus and incus, can still hear. Good hearing is often associated with a moist ear, the moisture acting as a false drumhead. This fact has been utilized in chronic cases with dry ears: these patients often hear reasonably well if a drop or two of glycerin or liquid paraffin is instilled into their ears at fairly frequent intervals.

Many patients with attic perforation, however, have for all practical purposes normal hearing, and it may be difficult to explain the need for operation to a person who hears well and has been unaware of any pus in his meatus.

Diagnosis

An inspection of the ear can be made either by directing light from a head-lamp or frontal mirror down a suitably sized aural speculum or with a self-illuminating auriscope (Fig. 2). The first method has the advantage of leaving one hand free for mopping out discharge or removing debris with a wax hook or forceps. Self-illuminating auriscopes give good and magnified vision, but both hands are required to manipulate them gently and it is therefore difficult to swab out or remove debris through them.

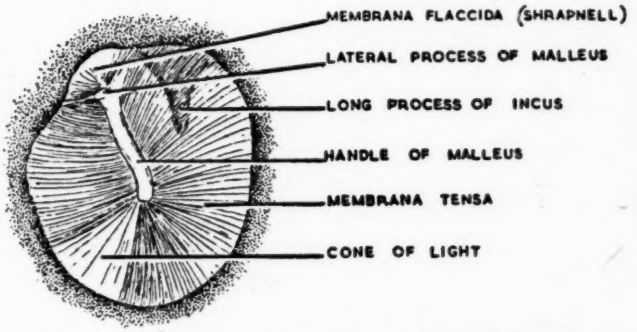

FIG. 2.—Appearance of normal left tympanic membrane.

It is most important to examine the second ear. If normal, it is a useful standard by which to judge the affected ear. It may, however, be diseased, although not complained about.

When there is much discharge or debris it is best to syringe out the meatus with warm lotion before attempting a detailed examination. If the meatal contents are

hard or impacted it may be necessary to soften them for several days before the meatus can be cleared. Glycerin, sweet oil, or a saturated solution of sodium bicarbonate is best for this purpose. Peroxide is not advised; it makes a frothy mess and results in a sodden meatal wall; the "fizzing" is often alarming and even painful to children and some adults. Badly impacted masses of epithelial debris may require instrumental removal under an anaesthetic. It is useless to try to make an accurate diagnosis until the meatus is clear.

As infected teeth, tonsils, adenoids, or accessory sinuses may contribute to tubal and hence to middle-ear infection, the need for their examination is self-evident.

A rough estimation of hearing may help to assess the extent of the disease and may influence treatment. Good hearing will always predispose to a conservative line of treatment if such can be undertaken safely. If there is no useful hearing radical surgery may curtail a long, tedious, and often unsuccessful treatment, without there being any fear of reproach for the destruction of function.

The old Ministry of Labour standard gives a useful rough classification. With the opposite ear occluded by a finger, not stationary but moving rapidly in and out at the entrance to the meatus, try a soft whisper, a forced whisper, an ordinary conversation, and a loud voice at 1 ft. (0.3 m.) from the tested ear, and grade 1, 2, 3, or 4 respectively according to which is first heard.

If a middle C tuning-fork (256 c./s.) is available compare air and bone conduction (Rinne's test) in both ears, and by placing the tuning-fork in the midline see if it is referred more to one ear than to the other (Weber's test). In middle ear deafness bone conduction is usually better than air conduction, and Weber's test is referred to the damaged ear (or worse ear if both are involved).

Polypi may present at the meatal orifice and thus be quite obvious. If deeper in the meatus they can usually be identified by the fact that they lie nearer the eye than the tympanum should, by their usually pink colour, their relative insensitivity, their mobility, and their tendency to bleed when touched or after syringing.

On the other hand, a red and bulging drumhead or swollen tympanic mucosa may be mistaken for a polypus. The first is an acute condition; a swollen mucosa is not insensitive to a probe, nor can a probe be passed around it.

Perforations vary considerably in shape, size, and situation (Fig. 3). They are often quite obvious, but, if not, their presence may be indicated by a granular margin, the protrusion of a bunch of granulations, or by a discharge. Attic perforations are often missed because of their high position.

A small perforation can sometimes be demonstrated by asking the patient to close the nose and mouth and blow out the cheeks forcibly; if the Eustachian tube is patent discharge will bubble through at the site of the perforation or air can be heard to squeak or whistle through it.

Masses of dead, white, greasy, and offensive debris protruding through a perforation or lying in the meatus usually mean cholesteatosis.

Many cases show periodic variations in the amount of discharge, depending on the weather, indulgence in swimming, recurrent coryza, etc., but an acute exacerbation of symptoms accompanied by mastoid tenderness must, as mentioned above, be regarded seriously. As a result of prolonged erosion thin barriers only may separate the infection from vital intracranial structures

The complications which may occur are labyrinthitis, cerebellar abscess, cerebral abscess, meningitis, lateral sinus thrombosis, and facial palsy. The danger signals have already been mentioned. The prognosis in all but the last has been greatly improved by the advent of chemotherapy and antibiotics.

Treatment

Prevention is Better Than Cure: Cure is Better Early Than Late

Acute suppurative otitis media of infants and children should be carefully controlled. Often a period of in-patient treatment is advisable, and it should be a maxim that no suppurating ear is lost from observation until the discharge has ceased and the drumhead can be seen to be normal again or the site of a dry, clean perforation. A child should not be discharged from a fever hospital with a running ear. Any recurrence must be reported and treated.

Reliance on chemotherapy and antibiotics without visual evidence of a return to normal is dangerous. Fever, pain, and often discharge may abate, but unless the drumhead is seen to recover its normal lustre and landmarks latent infection may still be present.

Failure to resolve may be due to upper respiratory tract infection, of the adenoids particularly, or to spread from the middle ear to the mastoid. In the latter event infection of the mastoid will not necessarily become acute and may settle down to become a chronic reservoir of infection.

If local toilet—probably gentle irrigation and dry mopping are best—fails to give a dry ear, operative treatment of infected tonsils and adenoids or lavage of an infected sinus should be considered, and the mastoid should be carefully

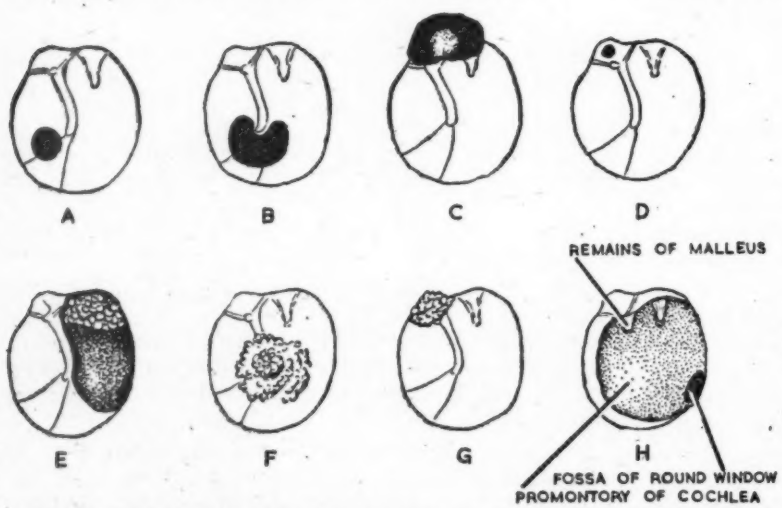

FIG. 3.—Clinical appearance of some common perforations of the left tympanic membrane. A, Antero-inferior perforation. B, Kidney-shaped central perforation. C, Extensive attic excavation, exposing the head of the malleus. D, Small perforation through Shrapnell's membrane. E, Posterior and marginal perforation with granuloma in attic region. F, Central perforation hidden by granulations. G, Granuloma hiding perforation through Shrapnell's membrane. H, Extensive loss of membrana tensa, showing bare bone of inner tympanic wall.

investigated. A radiograph may show unsuspected infection of a cellular mastoid, and a timely conservative operation may give both a dry ear and full hearing, and may save permanent damage which ultimately would have necessitated a radical operation.

In established chronic cases treatment may be conservative or operative.

Conservative Measures

In conservative treatment skilled cleansing is of paramount importance. This can be done by mopping under direct vision or, safely and painlessly, by syringing. Many solutions are used, but plain boiled water with or without sodium bicarbonate, 1 dr. to the pint (4 g. to 568 ml.), is as good as anything. The lotion should be used at body temperature, to prevent a caloric reaction of the labyrinth. After careful drying, 50 to 100% spiritus vini rectus can be instilled warm. If there is much discharge, this should be done daily or twice daily. Some prefer the so-called "dry treatment," and after cleaning they insufflate a powder such as boric acid (99 parts) and precipitated iodine (1 part), sulphathiazole, or sulphathiazole and penicillin.

Banham undertook conservative treatment in a number of Royal Air Force personnel with gratifying results. He preferred the dry treatment, and used sulphathiazole and boric powder in equal parts after trying several other combinations. Many cases were rendered dry and remained so while under observation for over 12 months. Causes of failure necessitating operation were mainly: (*a*) cholesteatosis which could not be removed through the perforation; and (*b*) marginal perforations with granulation, indicating necrosis of bone.

Granulations and polypi were not necessarily a bar to conservative treatment; these were removed under local analgesia (5% cocaine with a little 1/1,000 adrenaline). (Bonain's drops are probably more certain; they are composed of equal parts of phenol, menthol, and cocaine hydrochloride.) Cases with granulation tissue within the tympanum did not respond so successfully. Central, pre-central, and post-central perforations responded best.

If there was no improvement after two months, operation was advisable. Banham found that a high E.S.R. (20+) was an indication that conservative treatment might fail, and compared this state of affairs to that found in chronic osteomyelitis.

Banham's results were largely confirmed by Scott Stevenson and Ballantyne in a smaller series of cases in the Army. They suggested that, if after one month's trial the dry treatment failed, ionization should be tried for a further month and then operation should be considered.

Collins and Hughes found that local penicillin, with or without other chemotherapeutic agents, was of no value. Systemic penicillin is certainly of no value in chronic suppuration of the ear, except to resolve an exacerbation or control complications.

Operation

Operative treatment is the concern of the otologist. The aim is a dry safe ear, with the antrum and tympanum easy to inspect and with conservation of hearing. Of recent years the endaural approach has become popular; it certainly gives satisfactory results in a high proportion of cases, with the least disturbance of soft tissues, a safe approach to dangerous structures, and a good cosmetic result. A discussion of the various skin-flaps and modifications of the classical radical mastoid operation would be out of place here.

Even in long-standing cases clearance of upper respiratory infections should always be a first step. Sometimes it will render conservative measures successful, and it certainly improves the chance that a radical operation will succeed, with early healing and epithelization.

Any patient who has had a radical mastoid operation should submit himself for regular inspection and toilet ever after, though this may well be at increasing intervals. The epithelial lining of his cavity is not very secure on its bed of bone, and any accumulation of debris may well lead to ulceration, baring of bone, and the formation of granulation tissue. Careful removal of scales and crusts, cauterization of any granular areas, and the insufflation of a powder or instillation of spirit drops are all that is required.

TUBERCULOSIS HEALTH SERVICE

A conference largely attended by tuberculosis medical officers and tuberculosis visitors and nurses was held at the Royal College of Nursing on January 13 to discuss the present and future administration of the service.

Dr. PHILIP ELLMAN, who presided, said that since the Ministry of Health took it over the tuberculosis service had had inevitable teething troubles. The problem he found most difficult was that of divided responsibility. Preventive action was the sphere of the local authority, while therapeutic action was the sphere of the Ministry. Thus the health visitor was the servant of the local authority, but the chest physician the servant primarily of the Ministry and secondarily to some extent also of the local authority. Who exactly, then, was the health visitor's master? If the health visitor was to do her work properly she must not only visit the patient at home but also be present when the patient came to the chest clinic. No health visitor worth her salt was going to be content to visit the patient in his home without a full knowledge of his condition. Pulmonary tuberculosis was one of the few diseases in which the individual patient was not the only problem to be considered. The incidence in contacts was five times as high as in the population as a whole. Again, what was to be the attitude towards the early curable case in relation to hospital admission? It was all very well to say that the advanced case must take second place, but the question was whether the advanced case was going to be the source of a number of early cases. In the field of prevention it was necessary to educate not only the community but medical students and general practitioners. Why, therefore, should not chest clinics be used as educational centres?

The Waiting-list

Dr. G. E. GODBER, Deputy Chief Medical Officer, Ministry of Health, said that in the past they had become so used to the old organization of the tuberculosis service based on local government boundaries—which were inappropriate to clinical services—that they were slow to perceive its failings. Tuberculosis had been separated off from the general body of medicine to a degree which seriously hindered treatment. It was still the most pressing of our hospital problems. There were long waiting-lists for hospital and sanatorium beds, and to obtain admission to a sanatorium might take many months. Since July, 1948, additional beds had been made available—in general hospitals and their annexes rather than in sanatoria—and the number of nurses increased. The placing of tuberculosis beds in general hospitals made it easier to obtain staff. The important thing was that there should be some place where something could be done at once for the early case.

One of the most important advantages of the new administration was that the old isolation of the tuberculosis officer from his clinical colleagues had been ended.

The present position had its hopeful features. The complete figures for 1950 were not yet available, but the uncorrected weekly returns for the large towns showed during the last year a fall of some 18% in the deaths from tuberculosis as compared with 1949. Notifications, however, had increased, and it was not known with any certainty whether this indicated a true increase of the disease. During the last 20 years we had been passing from the near impotent watching of the patient to active treatment which gave to many sufferers if not cure at least arrest. But with a waiting-list of 11,000 it would be absurd to contend that we were satisfied with the present arrangements. He would claim only that the National Health Service Act was beginning to bear fruit in the improvement of quality and quantity of treatment, and that research had provided new means of treatment which should result in still more rapid progress.

The part of the family doctor in all this, Dr. Godber continued, was vital. Owing to the old structure of the tuberculosis service and National Health Insurance the general practitioner was very much in the background in the treatment of pulmonary tuberculosis. Yet upon his early diagnosis depended the success of treatment, and he it was who must supervise domiciliary treatment. They were all much too prone to forget the role of the family doctor in the control of tuberculosis.

He was not quite sure that the medical officer of health and the chest physician were co-operating as well as they might. The chest physician was not just another assistant medical officer, nor was the medical officer of health a sort of office filing machine to be fed with large quantities of statistics. Most of the individuals concerned had worked out a perfectly happy relationship, but the situation called for real effort from both.

Mass Radiography and B.C.G.

Mass radiography had been applied to about five million people during the last six years, and 18,500 had been picked out with active pulmonary disease. But the best use of mass radiography had not yet been found, and better facilities for the general practitioner (through whom the vast majority of cases were brought to light) might do a good deal more in accomplishing earlier diagnosis. The use of B.C.G. in this country was still in its early stages. The Medical Research Council had a trial in hand now, and scientific answers might ultimately be given to some of their questions. B.C.G. immunization was essentially a preventive service and was a matter for the local health authority. It was only the special nature of the vaccine which had hitherto kept it in the hands of chest physicians.

At the close of Dr. Godber's address the conference was thrown open to discussion. A special point was made by several speakers of the disadvantage of the doubling of functions by the health visitor and the tuberculosis visitor. One speaker said that the potential of the mass radiography service was some three million examinations a year. He was sure that the proportion of active cases detected was now much higher than the 5% of all notifications—the figure originally given. This speaker urged that there should be one mass radiography unit for each clinic area of 200,000 people.

Case Conferences

Dr. E. G. SITA-LUMSDEN, of Southend-on-Sea, said that in his town they had a weekly meeting with the medical officer of health, the school medical officers, the superintendent health visitor, the home health supervisor, the superintendent of home nursing, the chief sanitary inspector, and the children's officer. The purpose was to discuss all new cases and points of interest and importance in the old ones. Home treatment, B.C.G. inoculation, and isolation of contacts came before the conference. There was no friction, and very good results were obtained. By co-operating with the housing authorities, and being careful to recommend only cases which they considered urgent, they had secured a satisfactory proportion of new houses for families in which there was tuberculosis. Relatively few cases had been elicited by mass radiography, perhaps owing to the good liaison with general practitioners, who were encouraged to send any suspicious case or contact for further examination.

Common Lodging-houses

Someone having referred to the "scandal" of London lodging-houses as breeding-grounds of tuberculosis, Dr. W. HARTSTON (L.C.C.) said that the number of cases of tuberculosis in common lodging-houses inspected by the L.C.C. was not much greater than the incidence for the general population of London, though in this connexion the age distribution of the inmates must be remembered, a fair proportion being old-age pensioners. The L.C.C. had also made available lodging-house provision in which every tuberculous man had his own cubicle with its four walls so that he could not infect his neighbours. Arrangements had been made for priority of admission to be given to cases recommended by local chest physicians; further, if a chest physician considered that a patient should lie down in his bedroom for part of the day, this was permitted although the rule in common lodging-houses was that inmates must not occupy the bedrooms during the day. Two hostels were to be opened by the L.C.C. for homeless tuberculous persons, chiefly of the infective type, one in the country and the other in London, the latter for men still remaining in employment.

Training of Nurses

Dr. GODBER, replying to questions, said that the Ministry fully appreciated the importance of tuberculosis experience in the training of the general nurse, and a discussion was now taking place with some of the teaching hospitals on the possibility of seconding nurses to sanatoria. Some held that the general training of nurses would never be satisfactory until they spent some part of their time in a sanatorium. The key to this problem was the grouping of hospitals to form hospital centres, with a sanatorium as one of the group. As to tuberculosis visiting, most visitors were now on a whole-time basis.

He still felt that they must be a little critical in their approach to mass radiography. He was not decrying the work done in this field, but he thought it called for careful appraisal. The object of the tuberculosis service was not to pass the whole population three times a year in front of the minature radiographic apparatus. The better course was the miniature radiographic apparatus. The better course was to provide greater facilities for diagnosis by general practitioners.

One speaker had complained of lack of contact between chest physicians and health visitors. He himself was not an authoritarian, and he did not believe in the Ministry in Whitehall issuing edicts that things must be done in precisely this or that way. This liaison was a matter for the local authority. He had been impressed by the excellence of the Southend conference idea. There was only one omission from the list which the speaker had given, and that was the general practitioner, but perhaps it had been inadvertent. In conclusion he said that the ultimate solution of many difficulties was the inclusion of chest clinic facilities within the general out-patient department. They did not want isolated small dwelling-houses as chest clinics.

A meeting of the examining subcommittee of the Medical Artists' Association of Great Britain will be held on Friday, April 6, to consider applications for admission from intending members. A form of application for membership, including full details, may be obtained from the honorary assistant secretary, Miss Audrey J. Arnott, A.R.C.A., The Rotunda, The Radcliffe Infirmary, Oxford. All work for the examination must be sent to Miss Arnott, c/o Dr. Tompsett, at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, to arrive not later than Wednesday, April 4.

ANIMAL OR VEGETABLE PROTEIN

NUTRITION SOCIETY CONFERENCE IN LONDON

The Nutrition Society held a conference on January 20 at the London School of Hygiene and Tropical Medicine to discuss "The Comparative Merits of Animal and Vegetable Foods in Nutrition."

Professor R. C. GARRY, who presided, said that the pendulum of opinion on the amount of animal protein necessary for adequate human nutrition had been inclined to swing between extreme views. Early German work had first suggested that 120 g. of protein was required daily and that it might be of either animal or vegetable origin. Later Chittenden, in America, claimed that only 30 g. was required, but there was now some doubt about the reliability of his experimental evidence. Subsequent estimates suggested a round figure of 1 g. per kg. of body weight, and it was considered desirable that at least half the allowance should be of animal origin. Hindhede contended, however, that large amounts of animal protein were not only unnecessary but actually harmful; as evidence he pointed to the particularly good health of the Danes during the first world war when they were selling most of their meat to the warring countries and were themselves subsisting mainly on potatoes. Nevertheless many believed that a high consumption of meat had psychological and sociological virtues. "The roast beef of old England," which possibly had never existed in any very great quantity, was considered the basis of our national character as typified by John Bull. In view of the controversies which inevitably arose in discussions between meat eaters and vegetarians he predicted a stimulating and profitable conference.

Biological Values of Animal and Vegetable Proteins

Dr. G. R. TRISTRAM explained that the biological values of proteins as measured by their ability to promote growth depended on their containing adequate amounts of the essential amino-acids, which included tryptophan, phenylalanine, lysine, threonine, valine, methionine, leucine, *iso*leucine, and histidine. Although many animal proteins contained adequate amounts of all these acids a few did not; serum albumin contained no tryptophan, and haemoglobin no *iso*leucine. To some extent other components of the diet might influence amino-acid requirements, as when a liberal intake of methionine increased toleration of a diet high in fat. The biological values of some vegetable proteins might be reduced by poor digestion through the presence of cellulose.

Dr. K. J. CARPENTER showed how the biological values of various proteins, as found in growth tests with rats, agreed well with their chemical scores as judged by the resemblance of their amino-acid analyses to that of egg white, which was taken as the ideal protein. In making the chemical score it was only necessary to consider the amino-acid which showed the largest deficit in comparison with its concentration in egg albumin; the score was high when this deficit was small. In comparing the value of animal and vegetable proteins for pigs and poultry the problem was complicated by the high content of vitamins in "animal" foods such as fish meals and dried skimmed milk. With the introduction of alternative sources of these vitamins, such as synthetic riboflavin, condensed fish solubles, vitamin B_{12}, and by-products from the antibiotics industry, there was more scope for the use of suitable vegetable proteins. Research had shown that even when supplemented with vitamins vegetable meals made from groundnuts, coconuts, beans, and other sources were still inferior to equal amounts of animal meals. Good growth in animals given vegetable meals, however, could generally be secured by increasing the proportion of meal in the diet above the usual level.

Cattle or Corn?

Dr. K. L. BLAXTER first mentioned the important work of Rose on human amino-acid requirements, and then calculated how well these requirements, and those for vitamins and other nutrients, could be met by one acre of land used in various ways. Thus, if wheat were grown, 2.4 men would be supplied each year with calories, 2.4 with tryptophan, 1.8 with lysine, 2.1 with methionine, 0.3 with calcium, 3.8 with aneurin, 0.2 with ascorbic acid, and 0.1 with vitamin A. In contrast milk from dairy cows would supply 0.6 men with calories, 2.8 with tryptophan, 4.1 with lysine, 1.5 with methionine, 3.6 with calcium, 0.6 with aneurin, 0–0.7 with ascorbic acid, and 1.0–2.0 with vitamin A. By-products must not be overlooked; although sugar beet was a direct source only of calories the pulp rejected by the factory was a valuable cattle food.

Dr. D. A. BOYD discussed economic and statistical aspects of the production of animal and vegetable foods. Grass was the most efficient food for cattle and sheep, providing up to 20 cwt. (1,016 kg.) of starch equivalent per acre as compared with 14 cwt. (711 kg.) with grain, and with much less labour. In general about 10 units of energy had to be given to animals to get back one unit of energy for human consumption. Dairy cows and fowls were considerably more efficient in supplying protein than beef cattle, sheep, and pigs, but their management required much more labour. The prices paid to British farmers for beef and mutton were about twice those paid for imported meat. More efficient husbandry could increase meat production in this country, and a ratio of 6 to 1 between the food given to the animal and the food value of its carcass should theoretically be attainable.

Beef Tea and Bread

Dame HARRIETTE CHICK spoke on supplementary action between different proteins. Vegetable proteins tended to be low in trytophan and lysine, and high in cystine and methionine; for animal proteins these tendencies were reversed. In experiments with rats she had obtained justification of the time-honoured beef tea and bread as an easily digested meal for invalids. Gelatin in the beverage made good the deficiency of lysine in the bread. Other examples of supplementation had been found between the bran and endosperm of wheat, between wheat gluten and the non-protein nitrogen fraction of potatoes, and between the protein and non-protein nitrogen fractions of potatoes. During work for Unrra a mixture of soya flour, malt extract, and white flour had been found to be a satisfactory substitute for milk in young children.

Dr. LUCY WILLS described her work on "kwashiorkor," as observed in native African children weaned on to a diet of "samp" made from Kaffir corn, and also in adult Africans subsisting mainly on carbohydrates. The disease got its name from rusty-red pigmentary changes in the hair and skin. There was failure in haematopoiesis, liver disease, muscular wasting, and often skin disease. Waterlow had studied essentially the same syndrome in the West Indies; so probably had Czerny in Europe under the description of "Mehlnahrschadung." In her experience affected infants developed diarrhoea, followed by oedema, but sometimes by atrophy. The death rate in untreated cases generally was 11%, but almost all the atrophic cases died. Her oedematous cases were successfully treated by forcibly feeding them upon "naas," made from the curds of skimmed milk. Taylor and Chhuttani had demonstrated the value of animal protein as a protection against anaemia in adults; they had found an incidence of 58.5% among vegetarian Indian troops but of only 2.6% among troops eating meat.

Vegetable Substitutes for Milk

Dr. R. F. A. DEAN dealt with the important problem of devising adequate vegetable substitutes for milk. Most success had so far been obtained with mixtures containing soya meal, which was particularly rich in protein, but recent experiments with sunflower meal had been quite promising. In trials on 1–2-year-old children living in a German orphanage Dr. Dean and his colleagues had given a basal diet of semolina, potatoes and other vegetables, butter, and bread, which was supplemented in one group by milk and in other groups by a mixture of soya, wheat, and barley flours. The soya flour

given to some of the children had been steamed for a short time to remove its bitter taste, while others received flour steamed for a long period so as to destroy its trypsin inhibitor. The supplements with soya in either form had allowed growth at more than the standard rate for 8 or 16 weeks, but the flour heated for the longer period caused diarrhoea. In experiments with rats the addition of B_{12} to a vegetable diet containing soya flour was found to improve growth. This vitamin seemed worth a trial in the treatment of "kwashiorkor."

Dr. F. WOKES, speaking as a vegetarian, claimed that diets low in animal protein were capable of maintaining good general health. Dr. S. G. WILLIMOTT concluded from his experiences in a Malayan internment camp that it was possible for Europeans to subsist for long periods on diets as low in animal protein as those habitually consumed by natives in the Far East.

Nova et Vetera

A STORY BOOK

Eternal Eve. By Harvey Graham. (Pp. 699, with 20 plates and 20 other figures. 42s.) London: Heinemann. 1950.

This is a puzzling book and one difficult to review. It is of immense length, containing more than 700 closely printed pages and some 300,000 words—perhaps equivalent to a third of the printed matter in *Gray's Anatomy*. Its narrative is not very closely knit, and it is somewhat difficult to describe the contents; but it is, in effect, a history of gynaecology and obstetrics, with some tendency to stress the macabre and unsavoury. Its preface is dated both Cairo, 1941, and London, 1948, which suggests that it must have taken more than seven years to write. In view of the immense amount of material involved this is very easily intelligible. But the puzzle is why the book is designed as it is.

The preface says that "the reader should be an ordinary man or woman . . . for this is a story book." But few ordinary men or women could embark on such a shoreless literary ocean. On the other hand, detailed though the work certainly is, no historian, medical or other, can readily use it, since it has no references at all and a bibliography of under 40 items, most of them of a textbook character. Nevertheless the last hundred pages dealing with the modern period, for which exact reference, being easily accessible, is relatively unimportant, do certainly provide a spirited and extremely readable account of the scientific advances that have made childbirth safe. They would by themselves make an excellent, interesting, and deservedly popular volume.

The author exhibits great talents, and undoubtedly possesses much industry. He is master of a most attractive style and can draw on a remarkably extensive fund of information. He has obviously read widely. To the reviewer it seems, therefore, a matter for great regret that so rare a combination of powers should not be directed to a more defined end. Dr. Graham is an expert and polished exponent of medical thought to laymen, and he joins this with a lively interest in medical history and considerable knowledge of it. These are useful gifts. They cannot, however, be exhibited in the same book, and the very attempt to combine them makes them mutually destructive. There is ample room for a short book on the rise in the status of woman, based on an increasing knowledge of the true nature of sex, the scientific key to which—genetics—is, however, hardly touched on here. There is also a ready welcome from scholars awaiting a documented record of the history of sex-knowledge, but the documentation is here lacking. This book, seeking to reach both these ends, cannot be said to get very near to either. Dr. Graham can do many times better than that.

C. S.

Reports of Societies

COMPARATIVE BIOLOGY OF NATURAL FIBRES

The Comparative Medicine Section of the Royal Society of Medicine met on December 20, 1950, to discuss the "Comparative Biology of Natural Fibres." The meeting was well attended, and concluded with a useful general discussion and demonstration by Dr. Alexander and Dr. Bamford.

Professor A. HADDOW introduced the speakers, and Professor W. T. ASTBURY (Leeds) opened the discussion by reviewing current ideas on the structure and functions of polypeptides, polysaccharides, and polynucleotides. He developed the theme that these long-chain molecules are of great importance in living organisms because, as a result of their complex and highly organized molecular architecture, they possess both versatility and specificity.

Dr. K. M. RUDALL (Leeds) gave an account of investigations on the keratin in mammalian epidermis. By cytochemical methods he demonstrated the principal changes which take place during cornification—for example, the oxidation of −SH groups in the lower strata to form S-S groups in the stratum corneum. The condition of the fibrous protein in the stratum mucosum is analogous to that of fibrin in some of its properties, such as extractability in urea solutions. The isolated protein has the same temperature of transformation—for example, spontaneous change from the α- to the β-form in water—as the intact protein in the tissue. The temperature of transformation for the stratum corneum is about 20° C. higher than that for the stratum mucosum.

Dr. P. ALEXANDER (London) discussed the microscopic structure of a wool fibre and the arrangement and properties of the macromolecules composing it. Treatment of wool with peracetic acid oxidizes disulphide bonds and makes most of the material readily soluble. The small insoluble residue is identified with the subcuticular membrane, situated just below the scales, and giving in its natural state an *x*-ray diffraction picture of unoriented β-keratin. The greater part of the oxidized wool is soluble and can be separated into two fractions: α-keratose, which contains little sulphur, is electrophoretically homogeneous, and consists of spherical particles of molecular weight 70,000, and gives an *x*-ray diffraction picture of α-keratin; and γ-keratose, which contains more sulphur, is polydisperse, and has an average molecular weight of 4,500. Dr. Alexander suggested that the cortex of a wool fibre is built up of micelles of α-keratose imbedded in a cement of γ-keratose. Whereas breakage of disulphide bonds does not affect the α-pattern of the wool fibre, treatment with strong solutions of lithium bromide to break the hydrogen bonds changes the α-pattern to a disoriented β-pattern. The stability of the α-fold appears to be maintained largely by the hydrogen bonds, although disulphide bonds apparently contribute to this stability, because oxidized wool fibres or α-keratose are more easily changed to the β-form than is untreated wool.

Dr. C. H. BAMFORD (Maidenhead) described investigations on some synthetic polypeptides by polarized infra-red spectroscopy and *x*-ray diffraction, and discussed how the results help in understanding the proteins of living organisms. He suggested that in the α-form the polypeptide chain is folded into a series of 7-membered rings such that all the hydrogen bonds are satisfied intramolecularly; on changing to the β-form the 7-membered α-folds open up without rotation of the side chains and release the hydrogen bonds, which may then re-form with adjacent chains.

Professor J. T. RANDALL (London) gave a brief report of some investigations in the electron microscope of chromosomes and of the flagella of spermatozoa. Although the

interpretation of electron micrographs of chromosome material was very difficult, it would appear that the main axis of a lamp-brush chromosome from an amphibian oocyte was a fine thread only about 200 Å thick. The flagellum of a ram spermatozoon was a very complex structure containing a large number of fibrils which might differ not only in their arrangement but also in their chemical nature.

GOUT

A meeting of the Section of Physical Medicine of the Royal Society of Medicine was held on January 10, with the president of the Section, Dr. W. Yeoman, in the chair. The subject of discussion was gout.

Familial Factors

Dr. DONALD WILSON (Chichester), in opening the discussion, described the introduction of the term "gout" in the seventeenth century, when the Bishop of Chichester's secretary used it as a diagnosis of the condition of one of the Bishop's servants. The condition was cured by making the patient wear the Bishop's boots.

Dr. Wilson went on to give an account of his investigations into 77 cases of gout. These 77 cases were among 1,570 cases of arthritis seen during the same period—an incidence of 5.4%, which was a higher percentage than had been reported previously in other series. Fourteen of his cases (18%) had tophi. He had noticed that stress in one form or another appeared to be a frequent precipitating factor in the acute attack, and he had therefore investigated the family histories of his patients with special reference to the responses of other members of their families to stress. Compared with the families of patients with rheumatoid arthritis and monarticular (traumatic) osteoarthritis, he had noted that they were particularly liable to psychosomatic disorders. His figures suggested that the patient's disease, whether gout, rheumatoid arthritis, or osteoarthritis, was commoner than usual among other members of the patient's own family, and he had noted the high incidence of rheumatoid arthritis and peptic ulcer in gouty families. Dr. Wilson then showed the family trees of three gouty patients in which the incidence of hyperuricaemia was high. Peptic ulcer and rheumatoid arthritis also seemed abnormally frequent in these families. He concluded that members of hyperuricaemic families might react to stress by developing gout, but other members might react by having peptic ulcers, rheumatoid arthritis, or asthma. Finally, Dr. Wilson suggested that fluctuations of as much as 0.8 mg. per 100 ml. in the blood-uric-acid level might occur during the day. He concluded that the mechanism of the acute attack of gout was as yet ill understood, but that hyperuricaemia, stress, and possibly a vascular abnormality were all necessary before an attack developed.

Endocrine Aspects

Dr. D. H. COLLINS (Leeds) reviewed recent advances in knowledge of the endocrine aspects of gout. The work of Smyth, Stecher, Freyburg, and others suggested that the average plasma-uric-acid concentration was higher in males than in females, and that hyperuricaemia usually did not appear in affected males until puberty and in females until around the menopause. He also referred to investigations, using isotopic uric acid, into the size of the pool of miscible uric acid; these showed that this pool could be up to 25 times as large in gouty subjects as in normal people. A.C.T.H. and cortisone had been used to examine the endocrine disturbances in gout; these substances caused an increased excretion of urate and relieved the acute attack, although the therapeutic effect could not be explained entirely on this basis. Moreover, their withdrawal might provoke an attack of gout, which further suggested that there was a link between endocrine disturbance and the acute attack. This concept was strengthened by the findings of Wolfson and others of a low 17-ketosteroid excretion in gouty subjects.

Much more complete pathological information was available about chronic than about acute gout. Dr. Collins drew attention to the misconception that uric acid was deposited predominately in avascular tissue. While this could occur, uric acid was frequently found in vascular tissues, where it elicited a characteristic cellular reaction; typical examples of this were illustrated on slides, as well as the attrition of superficial cartilage, which also frequently occurred. Dr. Collins also demonstrated the effects of uric acid deposition in bone, leading to an osteitis and ultimately to resorption of bone. He concluded that the morbid anatomy of chronic gout was due to the uric acid deposits and that disturbance of pituitary-adrenal function, either intermittent or permanent, induced the pathological changes of acute and chronic gout.

Blood Uric Acid

Dr. R. M. MASON (London) said that the changes in the blood-uric-acid level in gout, and its limits in normal people had been insufficiently studied. Some had said that the level rose or fell just before an acute attack; others had claimed that there was no specific change. Hyperuricaemia could occur in conditions other than gout, and, although colchicine was recognized to be specific for the acute attack, it had no effect on blood-uric-acid levels, whereas atophan, which did have a specific lowering effect, was ineffective in acute gout.

He went on to describe investigations designed to clarify this problem, and showed the findings when daily blood-uric-acid estimations had been carried out under standard conditions. Two cases had been followed through an acute attack. In neither case were any specific changes apparent. Colchicine, which cut short one such attack, had had no specific effect on the blood-uric-acid levels. Atophan had been shown to bring the blood uric acid down to normal in other cases. In patients in whom gastro-intestinal disturbance has been induced by full "colchicinization" there had been a tendency for the blood uric acid to rise, presumably because of dehydration. The effect of operation (tophectomy) had also been studied, and it had been shown that a rise in blood-uric-acid levels occurred on the day after operation, although no acute attack had developed, and the level had then fallen to normal. Similar studies had been used in the diagnosis of doubtful cases, and Dr. Mason illustrated three types of curve which might be obtained. A high fluctuating level was characteristic of gout, and a low and constant level suggested that the patient was not suffering from gout. There was a third group of cases in which the blood uric acid fluctuated at or around the upper limit of normal, and in these cases such studies did not appear to assist diagnosis.

In the subsequent discussion, Dr. KERSLEY (Bath) quoted his experiences with 13 cases of gout in which plasma-uric-acid levels had been studied. He confirmed that colchicine had no specific effect on blood-uric-acid levels, whereas atophan and salicylates had, salicylates being slightly more effective than atophan. Glycine had no effect. Dr. RUSSELL-GRANT (Winchester) suggested that a fluctuating level of blood uric acid was more significant than a high one in indicating that a patient would respond to specific treatment. Dr. YEOMAN (Harrogate) quoted his experience that tophectomy often reduced the frequency of subsequent attacks, and Dr. HASSAN described his experiences with dogs which developed gout after strenuous hunting.

Dr. W. C. COPEMAN (London), in proposing the vote of thanks, pointed out how much information could still be obtained by clinical methods and observation, and that extensive laboratory facilities were not always necessary.

MANCHESTER AND LIVERPOOL PAEDIATRIC CLUBS

The second annual joint meeting of the Manchester and Liverpool Paediatric Clubs was held in Manchester on January 5, Dr. S. K. GUTHRIE (president, Manchester) being in the chair.

Adrenogenital Syndrome

Professor T. N. A. JEFFCOATE (Liverpool) read a paper on the adrenogenital syndrome, which he divided into two groups—the first being intrauterine in origin and resulting in pseudohermaphroditism from adrenal cortical hyperplasia, while the second occurred before puberty in children who had been normal in infancy. This group, in females, gave rise to virilism and was usually due to an adrenal cortical tumour. Professor Jeffcoate described a case in which such a tumour was removed and transplanted into a patient with Simmonds's disease. There was marked improvement in the recipient's condition until the graft died about six months after implantation, when symptoms recurred.

In deciding the correct sex in pseudohermaphroditism the value of 17-ketosteroid excretion was discussed, as was the most appropriate age for laparotomy in cases where doubt about the sex still existed. Professor Jeffcoate referred to the unsatisfactory results following removal of a hypertrophied adrenal gland and also mentioned the lack of dramatic change after extirpation of an adrenal tumour. Treatment of virilism had not so far been very successful, but clitoridectomy might be of value aesthetically.

Dr. B. WOLMAN (Manchester) discussed the successful use of cortisone in the treatment of the adrenogenital syndrome. Clinical improvement did not occur till between two and three months after beginning treatment. It might be possible to reverse the symptoms of virilization: control had certainly proved possible. Cortisone suppressed the excessive production of androgen by causing morphological involution of the adrenal cortex and depression of endogenous A.C.T.H. formation. Charts were presented showing the fall in output of 17-ketosteroids in patients under cortisone treatment—occurring within two days of the start of treatment—and the value of A.C.T.H. as a check on the suppressive effect of cortisone was clearly shown. A.C.T.H. caused a prompt rise in 17-ketosteroid excretion until cortisone suppression was adequate: thereafter it was without effect on the excretion.

Hypofunction of the Adrenal Cortex

Dr. R. McL. TODD (Liverpool) discussed the clinical, biochemical, and pathological features of hypofunction of the adrenal cortex in infancy, and described three cases. There was evidence to support the contention that each of the three layers of the adrenal cortex produced a hormone, excess or deficiency of which gave rise to a definite clinical syndrome. The outer layer (glomerulosa) was thought to control water and electrolyte metabolism, the middle layer (fasciculata) influenced sugar, fat, and protein metabolism, and the inner layer (reticularis) promoted masculinization and nitrogen anabolism. Hypertrophy of one zone might give rise to pressure atrophy of another zone, particularly of the zona glomerulosa; thus anatomical hypertrophy of the adrenal cortex might be associated with physiological hypofunction.

The three cases described were males who were admitted to hospital before 6 weeks of age because of anorexia, projectile vomiting, constipation, and failure to gain weight. Visible gastric peristalsis was marked. Recurrent dehydration necessitating repeated intravenous or subcutaneous infusions was a characteristic feature, the blood urea was raised, the carbon-dioxide combining power was low, serum sodium and chlorides were diminished, serum potassium was raised, and there was an increased excretion of urinary chloride. In two of the infants the adrenal glands were enlarged (weight 25 g.), and in one the adrenals were smaller than normal. Microscopically the zona glomerulosa in each case was found to be narrowed, thus supporting the contention that water and electrolyte metabolism was controlled by this zone.

Enlargement of the Thymus

Dr. EDITH PATERSON (Manchester) and Dr. BLAIR HARTLEY (Manchester) discussed the diagnosis, clinical and radiological respectively, of enlarged thymus and thymic tumours in infancy. Dr. Paterson reported a case of carcinoma of the thymus and mentioned the occasional occurrence of enlargement of the thymus in the early stages of leukaemia with prompt, but only temporary, response to irradiation. Five cases of enlarged thymus were described which had responded promptly and permanently to irradiation.

Dr. Hartley outlined the radiologist's difficulties in diagnosing mediastinal shadows as being thymic. The enormous variation of the shadows with the phase of respiration, the cardiac cycle, and effort (crying or struggling) made interpretation a hazardous undertaking in infants. In addition to skilled radiography Dr. Hartley stressed the need for several exposures (A.P., P.A., and lateral, all in inspiration) before any firm decision could be reached.

Correspondence

Appendicitis at Sea

SIR,—I am in entire agreement with Admiral Sir Sheldon Dudley's letter (January 20, p. 136). I have been at sea for 25 years and, while growing older, hope that I have also become wiser. During this period my practice as regards acute appendicitis has undergone a complete change. When I was younger and first went to sea I was inclined to operate on every case of acute appendicitis. I have gradually come to the stage where, except in the case of young children or the aged, all cases are treated at sea by the expectant method up to 24–30 hours. At the end of this period a decision is made whether to operate or to continue with expectant treatment. But should the patient during this time become worse—i.e., rising pulse rate, increased rigidity and pain, recurring vomiting, etc.—operation is carried out without waiting for 24 hours to elapse. Even before the days of antibiotics and chemotherapy most patients made an excellent recovery when treated by this method, and could then have an appendicectomy later under ideal conditions.

Admittedly, if an operation has to be carried out at the end of 24 hours the delay has increased the difficulty, as the tissues are more hyperaemic and friable, but, in view of the large majority of operations avoided at sea, this practice is considered justifiable.

I think that a definite time limit (e.g., 24–30 hours) must be set, as if one waits much longer the time to operate with safety will have passed. However, most cases will be settling down in 24–30 hours if they are going to do well.

It requires much more courage and judgment on the part of the surgeon to refrain from operating until expectant treatment has been given a trial than to advise an immediate operation in all cases.—I am, etc.,

Orient Steam Navigation Co. H. M. ROYDS JONES.

Appendicitis

SIR,—Sir Cecil Wakeley and Mr. Peter Childs (December 16, p. 1347) are to be congratulated on the excellence of their run of results in cases of appendicitis. It is not altogether certain whether this depends so much on their methods as on the care and skill with which the methods have been applied. Fully developed general peritonitis is, of course, the killer, and of such cases they had eight. To save all of them was a worthy achievement, but whether the figure is large enough to gladden the heart of a statistician I do not know. Certain points have already been taken up by other correspondents, but I feel that two comments should be made lest the very excellence of the reported

results should do harm rather than good. First, it is to be hoped that others will not be diffident about reporting failures because of this triumphant series of successes. It seems that I differ from many of my surgical colleagues in that I have had a death from appendicitis within the penicillin era. The case taught me more than my successes had done, and I feel that one fatality may be more informative than many a successful run. The patient was a man of 58 years who was admitted with general peritonitis from what turned out to be a perforated appendix, which was removed. He had all the advantages of sulphonamides, gastric suction, intravenous fluids—and penicillin. Admittedly the penicillin was not given until the fourth post-operative day, but the other adjuvants were used from the start. The patient died on the twelfth day of his peritonitis. There was no other contributing disease; he had been a healthy, strong man. The case caused me to scrutinize all the details of management, and one change was made. Since that time any complicated case has been treated by me from the outset with sulphonamides and streptomycin. On theoretical grounds penicillin is not an antibiotic of choice for coliform peritonitis. In so far as it may produce false confidence, I think it should not be given the emphasis that has been awarded to it in the article. If there is an indication for antibiotics one ought to give the best one available, and penicillin is surely a broken reed for this particular purpose. Your annotator (December 16, p. 1376) might agree with this, though his statement is not so emphatic.

There is one small point, too, about ordering sulphonamides. If the patient is on gastric suction they must be ordered to be given parenterally: otherwise we shall find ourselves giving the credit for improvement in results during the "sulphonamide-penicillin era" to the anaesthetists—but that might not be such a bad idea.—I am, etc.,

Northolt, Middlesex. E. A. TURNER.

SIR,—The article by Sir Cecil Wakeley and Mr. Peter Childs (December 16, 1950, p. 1347) makes me look back over forty years on my own view of the treatment of appendicitis.

I well remember, in 1908, being told by the late Sir David Wilkie of his vacation at the clinics of Kummel and Curacoa Kummel operated on all cases of appendicitis and Curacoa was a physician who treated all his cases with castor oil, but the mortality rate in each case was the same. The next impression I obtained of the treatment of appendicitis was when I became a house-surgeon to the late Sir John Lynn Thomas in 1911. He was a disciple of Murphy, of Chicago, and treated all his cases by the Ochsner-Murphy drip method. All went well until a nurse, aged 19, died, and afterwards all cases were operated on, especially since Moynihan expressed his view that a purgative often caused perforation of the appendix.

After this I had experience in general practice, and in one week saw three deaths from appendicitis, all of which were operated on in their own homes by a consulting surgeon: operation had been too long delayed. Following this a small cottage hospital was built, containing 26 surgical beds. I was appointed surgeon and was able to operate on all cases.

In the period 1925–46 I performed 800 operations with a mortality rate of 0.5%, and from 1946 to date I have performed 600 operations without a death. I operate now on all cases once a diagnosis is made. My method of treatment is the same as that adopted by Wakeley and Childs, except that I give anti-gas-gangrene serum and penicillin intramuscularly in all acute cases. In my opinion anti-gas-gangrene serum is a real life-saver. I have no waiting-list, as I consider it is too dangerous to leave any case without operation, since I believe it is impossible to know when a case will not flare up. Anaesthesia with thiopentone, gas and oxygen, and curare makes the operation simple and a pleasure to perform.

I have noticed that acute appendicitis is often associated with acute tonsillitis, and I have no hesitation in removing the appendix in spite of the tonsillitis. Penicillin treatment permits this. I had one case of Crohn's disease in which I removed the appendix. The case did well in spite of the fact that there was severe involvement of the ileum. I had two cases of Meckel's diverticulitis, both of which recovered and in which I removed the diverticulum.

The onset of gastric and duodenal ulcers as a result of recurrent attacks of appendicitis is not fully appreciated. I myself developed a duodenal ulcer and had a gastro-enterostomy performed at the age of 50. I recollect attacks of abdominal pain off and on since childhood. My appendix was removed and found to be fibrosed and adherent. This was the cause of my pains and probably of the ulcer.

With the knowledge that the public have of appendicitis it is imperative that operation should not be delayed, and after forty years' experience as a general practitioner I do not hesitate to recommend operation in every case of appendicitis. My work has been considerably lightened since I have adopted this treatment. Night and emergency calls are lessened.—I am, etc.,

Treorchy, Glamorgan. FERGUS ARMSTRONG.

Tonsillectomy

SIR,—It is to be hoped that the judicial approach of Dr. A. H. Gale in his able article (January 20, p. 133) will stimulate a like attitude generally. There is, for instance, an obvious disparity between the general anxiety to avoid tonsillectomy in a poliomyelitis epidemic (four deaths in 1949 under these circumstances) and the cheerful acceptance of the ordinary risks of the operation (80 deaths a year, according to Dr. Gale). May I add one comment concerning that large group of potential subjects for tonsillectomy, young schoolchildren of 5 to 7 years who suffer from recurrent upper respiratory infections. If to these one applies conservative measures, one quickly learns what the natural history of the syndrome is—that it is usually self-limited, with a marked tendency to spontaneous cure at about 7 or 8 years. Therefore decision about operation on this group of young schoolchildren should be postponed as long as possible. Since at most centres there is in any case a delay of many months before a booked tonsillectomy is performed, it would be well worth while to assess each child's need for operation again as his turn approaches. If this were done I believe many of these children would end by keeping their tonsils.—I am, etc.,

Cambridge. DOUGLAS GAIRDNER.

SIR,—Dr. A. H. Gale's article (January 20, p. 133) on pros and cons of tonsillectomy brings this perennial problem once more into the limelight. He is to be congratulated on its concise wording and its brevity. I believe statistics on this subject, as in many others, are not to be trusted; so many data are not available, and many who rely on statistics have some axe to grind. Dr. Gale quotes Kaiser's definite indications for tonsillectomy. Nos. 1–5 are. I would suggest, indications for adenoidectomy rather than tonsillectomy, and No. 8 should be excluded, at least until appropriate non-operative treatment for sinusitis has been given. I agree that Nos. 9–12 are very indefinite indications.

Dr. Gale might have said more on the subject of enlargement of tonsils. It is my experience that many practitioners regard enlargement as *the* indication for tonsillectomy. This is definitely not so, and in fact it is more often the small adherent buried tonsil which harbours the organisms responsible for chronic adenitis or recurrent tonsillitis. In his conclusion, Dr. Gale says the decision should be made by the general practitioner and the laryngologist, working together. I heartily agree with this. Unfortunately, very many of the cases referred for opinion come not from the G.P. who knows the medical history of the patient, but from the school medical officer, who of necessity sees the child only when well enough to attend school and, judging from the wording of most requests, regards enlargement as the chief indication.

It is to be hoped that the critical surveys encouraged by the poliomyelitis controversy will enforce more rigid selection of cases, for not only is the bed allocation small, but there is a real danger of laryngologists becoming pure tonsillectomists now that the regional boards are directing more and more of these operations to specialists away from

the G.P.s who have been doing them for many years. That, however, is another controversial point, upon which I must not expand here.—I am, etc.,

Exeter. PHILIP SCOTT.

SIR,—Few of us will fail to applaud Mr. C. Hamblen-Thomas's plea (January 6, p. 38) for the provision of greatly increased facilities for convalescence in the country for the city child, but one may well question the claim that the benefits of such treatment would be proportionately less costly than those of hospitalization for a timely tonsillectomy. Such Utopian projects, however desirable, must be pursued in relation to the economic health of the nation, and cannot reasonably be expected for many years.

There is no doubt that the operation for the removal of tonsils and adenoids is often regarded with excessive enthusiasm by profession and laity alike in treating the respiratory ills of childhood, but I believe that unnecessary operations are not commonly undertaken. I believe that the failure to deal adequately with the tonsil problem must inevitably have long been considered with concern by those responsible for advising and administering the Health Service. We can hope that they will eventually be successful, preferably along the lines suggested by Mr. Hamblen-Thomas, but the multitude of pressing problems facing a service already suffering from financial malnutrition would indicate that it cannot be hoped for soon.

In the meantime, an immediate solution is required. This solution can only be increased facilities for operation, and should be provided on a private basis, working complementary to the present arrangements. There are many parents who will always elect to have such operations on their children carried out privately. We must all be aware of cases where parents seek private treatment, facing the inevitably increasing nursing-home charges for no other reason than to expedite treatment which they have been advised is necessary, depriving themselves of television sets and cigarettes for the sake of their children. In a free society a demand must be met. It would indeed be interesting to know how many parents of children now on pathetically long waiting-lists for hospital attention and quite unable to consider seeking private attention would be willing, eager, and well capable of meeting an inclusive fee of, say, five guineas in order to have the operation completely and expeditiously performed.

I feel that it should not be beyond our enterprise to satisfy this need. I visualize units of ten to twelve beds, adequately staffed by nurses, under the control of a team of surgeon, anaesthetist, and general practitioner, operating by dissection three times a week. Only cases already on waiting-lists would be accepted and complicated cases excluded. By adhering to a strict and streamlined routine, with a well-organized escape route for complications, such an organization would surely be economically sound, with a resultant reduction of pressure on our overworked hospital beds.

Such a plan may in some ways be open to criticism. Perhaps our Health Service will soon solve our problems, but otherwise it may be left for private enterprise with its increased flexibility in facing local conditions to continue to operate complementarily to national schemes, to the greater benefit of the community.—I am, etc.,

Birmingham. NORMAN L. CRABTREE.

Physics of Breathing

SIR,—I cannot let go unchallenged a statement by Mr. G. Jackson Rees in his paper on "Anaesthesia in the Newborn" (December 23, p. 1419). He attempts to apply Poiseuille's formula, in order to relate resistance to respiration to the diameter of the trachea. Poiseuille's formula is, however, quite inapplicable, for the following reasons:

1. Poiseuille's formula deals with flow through capillaries. The sizes of trachea considered vary between 3.6 and 20 mm., and are not, therefore, of capillary dimensions.
2. The capillaries considered in deducing the formula are assumed to have inelastic walls, an assumption not applicable to the neonatal trachea.
3. The formula applies only to liquid flow—i.e., flow of an incompressible fluid—and is certainly not applicable to the flow of anaesthetic (gaseous) mixtures.

In fact the application of Poiseuille's formula gives rise to two statements in the paper which are difficult to reconcile. For on the one hand it is stated that application of the formula shows that to produce a given flow rate through the infant trachea, as compared with the adult trachea, a 256-fold increase in pressure is required. Yet it is stated that the resistance to inflation is very much less in the case of the infant lung. Although I realize that a good many factors are involved (muscle tone is specifically instanced), it is difficult to see how they could offset the 256-fold resistance to be expected if Poiseuille's formula were applicable.—I am, etc.,

London, N.4. G. HALEK.

Foetal Asphyxia

SIR,—Your leading article on the prognosis of foetal asphyxia (January 6, p. 23) would, I think, have been all the better if it had given some weight to the experimental work which throws light on the problem. I refer to Sir Joseph Barcroft's researches on the development of respiration in the foetal sheep, first, I think, communicated to the B.M.A. Annual Meeting at Aberdeen. There still seems to be appalling ignorance among obstetricians about this investigation into one of the fundamentals of their work, for in 1949, at the B.M.A. Annual Meeting, I looked at every book on obstetrics that I could find in the exhibition and only one, I think, made any reference to his work, and that was not very helpful. Even in America the brilliant work of this great investigator seemed to have been overlooked, and here to judge from the textbooks I saw, students are also kept in ignorance.

May I, therefore, once again give a brief résumé of the facts established by Barcroft for the sheep, which clinical observations suggest apply also to human beings? Barcroft's investigations showed—and the film he showed at Aberdeen illustrated it beautifully—that the first intrauterine respiratory movements came only from cutaneous stimulation in the nasal region, and that this area rapidly enlarged so that later on stimulation anywhere would initiate them. By this time asphyxia would have a similar effect, but a short while before term complete asphyxia, caused by clamping the cord, would not cause respiratory movements, while cutaneous stimulation would do so immediately. He also showed that as a result of several factors the central blood of a foetus shortly before term contains an astonishingly low concentration of oxygen, an observation which makes it most unlikely that simple asphyxia neonatorum would have any deleterious effect, thereby supporting the conclusion to which your article inclined.

Now for some of the practical conclusions to which Sir Joseph's work leads, about which I corresponded with him intermittently from 1939 till a few days before he died. The first and most important is that the newly born foetal brain is so nearly asphyxiated that oxygen lack cannot be the cause of the first breath. This is almost certainly caused by some cutaneous or other stimulation. If the baby does not breathe it is because, for some reason, the brain is not responding to the stimuli being received. The appropriate remedy is either to increase the external stimulation (Sir Joseph pointed out that normally a lamb is dropped on its nose, which is the first area to show a respiratory reflex on stimulation) or, if that fails, to give something which will lower the cerebral threshold—i.e., something allied to a convulsant. Our fathers and grandfathers used to inject strychnine, but, as I discovered accidentally many years ago, "cardiazol"-ephedrine works better than anything else I have tried.

The widely popularized view that a baby in white asphyxia is suffering from "shock" is therefore quite wrong, unless one makes the reservation (which is confusing) that the baby is suffering from pure nervous shock, while nervous shock is mainly vascular. The treatment demanded is quite different, and in view of the fact that the newborn baby is normally asphyxiated there is no reason to fear that even complete apnoea for 15 minutes will be followed by ill results. The one child I had like this, who began to breathe after 0.5 ml. cardiazol-ephedrine intramuscularly and

1.5 ml. into the left ventricle, developed quite normally till he had a severe attack of poliomyelitis 16 months ago.

To come back to your leading article, any cerebral damage will almost certainly not be due to ordinary asphyxia neonatorum, and to use 2, 3, or 5 minutes before breathing commences is a wrong criterion. Much more important from the point of view of cerebral damage is likely to be the time that elapses before vigorous breathing and oxygenation occur, for while the brain at birth seems conditioned for asphyxia it by no means follows that this continues when respiration has started. For example, it is quite safe to give 1 ml. of cardiazol-ephedrine to an asphyxiated infant (and even larger doses in cases of necessity), but soon after respiration has commenced half this dose will cause a convulsion. Therefore, to give some drug which will promptly initiate vigorous respiration is not meddlesome: it is probably the greatest safeguard against any mental deterioration developing as the child gets older, as well as against atelectasis or pneumonia.

As I have previously pointed out, this work has also important bearings for adult pathology, for it is probable that even where the normal oxygen regulation of respiration is failing, or has failed, the primitive response to stimulation remains. This is the justification for our fathers' faith in strychnine as a respiratory stimulant, for they used it in just such conditions, and I recorded a case of a boy, submerged for 10 minutes, in whom artificial respiration had no effect but who responded at once to a large dose of strychnine and vigorous slapping on his buttocks; in fact he was so near having strychnine convulsions that it needed two men to hold him on the stretcher while being transported to hospital, where he finally made an excellent recovery.

I wonder whether some writer will at last begin to put the truth into some textbooks so that our students may be taught what one of our greatest experimental physiologists discovered, and thereby many infant lives be saved.—I am, etc.,

Winsford, Cheshire. W. N. LEAK.

Congenital Abnormalities

SIR,—In your annotation of January 20 (p. 130) you mention inquiries into the causation of congenital abnormalities. May I suggest that no such inquiry is complete unless it tries to correlate the baby with the mechanical conditions of the pregnancy which produced it?

As regards the mother, it is important to know:

(*a*) Her sensations during pregnancy, as to discomfort, pain, or abnormal position of the foetus. Comparison with a pregnancy of hers that produced a normal child is most valuable.

(*b*) The amount of movement of the baby.

(*c*) The size of her abdomen. Such remarks as that "all the neighbours were surprised when I had a baby" should be noted.

(*d*) Difficulties with turning the baby because of malpresentation.

(*e*) Amount of amniotic fluid and when it came away.

As regards the baby, the points are:

(*a*) Posture into which it automatically folds directly after birth.

(*b*) Presence, situation, and depth of "pressure dimples," or their absence.

(*c*) Presence and distribution of stiffened joints.

(*d*) Presence and distribution of atrophied muscles.

(*e*) Presence and distribution of "moulding deformities," specially noting the situation of convexities fitting the concavity of the uterine wall, and the occurrence of "mutual deformities" which fit each other.

You mention at length the interesting inquiry, centring on deformities of the nervous system, carried out by Record and McKeown. Had they done as I have suggested, they would have found a definite group of cases showing the terrible syndrome of lumbar spina bifida, hydrocephalus due to the Arnold–Chiari deformity, irregular talipes, stiff joints, and undeveloped muscles in the legs. Everything about them and their histories would have suggested that from very early in pregnancy they were expanding against abnormal resistance, showing that they were what I call "compression babies."

The trouble about getting the mechanical factor in congenital abnormalities considered is that it is the business of no one in particular to examine the evidence, which is complicated although (I consider) convincing. Obstetricians, paediatricians, pathologists, and embryologists all consider it outside their work, and I am told that in many postgraduate orthopaedic classes to raise the question of the moulding origin of talipes elicits a snub, but no discussion of aetiology. However, if anyone is interested in the syndrome I have mentioned, I should be pleased to show him cinematograph records suggesting strongly a compression factor in the condition. And, although it is outside the scope of this letter, if anyone investigating congenital deformities can give me information about the presence or absence of hydramnios in cases of arthrogryposis I shall be most grateful.—I am, etc.,

London, W.1. DENIS BROWNE.

SIR,—Over 50 years ago Féré[1] showed that various chemical substances injected into eggs or applied as gases round the shell modified the development of the chick embryo. The results were demonstrated to be related directly to the toxicity of the substances used. Specific deformities could not be attributed to the chemical composition. Féré concluded that the effect of chemical agents depended largely upon the time of action and that the same injurious factor might cause sterility, monstrosities, abortion, stillbirth, or congenital deformity, according to the developmental stage at which injury occurred. Stockard in 1921[2] confirmed this, showing that a typical anomaly could be produced by several different agents. The primary response of the developing embryo to all effective substances was retardation of the rate of development, the most severe effects occurring in the tissues competent at the particular period of development.

Since then, no further evidence has been adduced to justify the application of the results of such experiments to particular human deformities such as congenital dislocation of the hip, arthrogryposis multiplex congenita, pseudarthrosis of the tibia, clubfoot, and osteogenesis imperfecta,[3] particularly as these deformities in humans are not associated with any stunting of growth or generalized skeletal abnormality (apart from osteogenesis imperfecta), such as the chick shows experimentally. This stunting of growth is an invariable feature of experiments with insulin and other noxious materials, whereas the occurrence of oversized and postmature giant babies has been frequently noted in diabetic women. Any comparison must therefore fail at this stage of our knowledge apart from the application of broad principles.

Other investigators[3,4] have noted that the increased birth weight, cardiomegaly, hyperplasia of the adrenal glands, and increase in eosinophilic cells in the anterior pituitary found in infants of diabetic mothers occur also in infants whose mothers were non-diabetic at the time of delivery but who developed diabetes later. Insulin-treated as well as prediabetic women are apparently in a border-line state of endocrine deficiency which permits better reproductive activity. Their pregnancies, however, are often interrupted by embryonic and foetal death, and among the offspring of such mothers there is an increased incidence of malformations.[3]

The interaction of genetic and environmental factors in the production of congenital deformity is fully established and recognized, but it fails to explain a large number of deformities which appear to be distortions rather than the result of aplasia or dysplasia. Spatial impairment, whether induced by genetic or environmental factors, is receiving more attention recently in this connexion, and any tendency to relate certain well-defined congenital deformities unassociated with generalized disturbance to gross experimental results must be regarded as a retrograde step.

Dr. P. K. Duraiswami's experiments[5] are of undoubted interest, but as the deformities described are always associated with a general systemic disturbance any application to orthopaedics cannot be justified, as he surely means to claim when

he uses phrases such as "adduction deformity resembling clubfoot," "the favourite site for pseudarthrosis in children," and "deformity of the limbs as seen in arthrogryposis."—I am, etc.,

Sheffield. GAVIN C. GORDON.

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Transfusion in Leukaemia

SIR,—There is general agreement that transfusion exerts no curative effect in leukaemia. In incurable malignant disease, lymphadenoma, and leukaemia transfusion is justifiable only for a particular purpose, such as to strengthen the patient to undergo special treatment—e.g., deep *x*-ray therapy. In the fatal case reported by Drs. P. D. Bedford and L. G. Lajtha (January 6, p. 38) the patient, who suffered from monocytic leukaemia, received 35 pints of blood in exchange transfusion, and, since transfusion has no curative effect in leukaemia, the transfusion was presumably given for some other purpose. Others may wish to use either simple or exchange transfusion in leukaemia and if so it should be borne in mind that any good effects achieved will be temporary; no cure can be hoped for by transfusion.

The assurance is constantly given to donors that blood they donate will be used only when it can do good and that every effort will be made to avoid needless transfusion and wastage. It is obviously important that these assurances be borne out in practice, particularly as in this country the blood donor never has received and does not receive a penny for his or her services. There are not lacking those who are ready to say blood is used unnecessarily or wasted in hospitals, and such opinions can adversely affect donor recruitment. At present more donors are needed all over the country, for the consumption of blood is still increasing.

Blood transfusion is a relatively expensive form of treatment. For example, the collection of 35 bottles of group A or group O blood will require the attendance of some 70 to 80 donors, in some instances at much personal inconvenience. A doctor, clerk, and four or five nurses will be occupied three to four hours bleeding these donors. The hall used for the bleeding session must be paid for and money expended on publicity, transport, drivers, etc. It still occasionally happens that blood banks are completely emptied. Also it is unfortunately occasionally necessary because of depletion of stocks to ration blood, with the consequence that patients who will derive real benefit from transfusion—e.g., cases of haemorrhage in childbirth, or haematemesis from gastric ulcer—may receive inadequate transfusion, or transfusion must be deferred till more blood is available.

These points serve to emphasize that blood is a valuable and expensive commodity. Tremendous good can be done with it. It is very desirable to consider carefully whether the patient will be helped by transfusion, and only to use it when benefit will accrue or may reasonably be expected. Transfusion should in fact not be given unless there is a special indication for it. Expense is hardly an item a doctor should reasonably be expected to consider if it is known that a particular form of treatment is the right one. On the other hand, if there is virtually no prospect of any benefit being derived from it, it is reasonable that the expense of the proposed treatment be considered in deciding whether it should be used, especially in these days of rising expense.—I am, etc.,

Cardiff. R. J. DRUMMOND.

Effects of Intravenous Citrate

SIR,—Drs. P. D. Bedford and L. G. Lajtha (January 6, p. 38) are to be congratulated on their warning of the possible dangers of large intravenous doses of sodium citrate in exsanguino-transfusion, which is now becoming a not uncommon procedure in the treatment of erythroblastotic infants and, as in their case, in leukaemia. Their patient received a total of 35 pints (19.6 litres) of blood in the course of six hours. Blood collected for transfusion usually contains as much as 2 g. sodium citrate in every pint (560 ml.); it follows, therefore, that the amount of citrate administered was approximately 70 g.

I have no personal experience of the biochemical effects of so large a dose as this, but in the course of experiments on citrate metabolism I have received an intravenous infusion of 250 ml 2.5% sodium citrate in a period of thirty minutes—i.e., 6.25 g. sodium citrate at approximately the same rate of infusion as in the case described. This comparatively small dose resulted in tetany and extremely severe and temporarily disabling headache for one hour following the infusion. The serum citrate concentration at the end of this injection was 30 mg. per 100 ml., which is approximately ten times the normal value. Less than 20% of the citrate was excreted in the urine, the remainder being rapidly destroyed by oxidation, so that normal levels were regained within one hour. It would appear probable that this speed of infusion is greater than the capacity of the body to remove citrate, so that it is likely that far higher concentrations were reached in the cited case. In addition, the excess cation remaining in the blood stream following oxidation of citrate results in a metabolic alkalosis which can be corrected only by excretion of excess sodium bicarbonate in the urine.

It would appear, therefore, that exsanguino-transfusion should always be subject to strict biochemical control if it is to be a safe therapeutic procedure. The two essential investigations for this control are estimation of the alkali reserve of the blood and the serum citrate concentration. The former is a standard laboratory procedure and the latter is a comparatively simple estimation if the pentabromacetone method is used (F. E. Hunter and L. F. Leloir, *J. biol. Chem.*, 1945, **159**, 295). In this therapeutic procedure there is of course no difficulty in obtaining blood for the analyses, as it is being constantly withdrawn from the patient. It follows, therefore, that exsanguino-transfusion is suitable only for a well-equipped centre where a competent biochemist is available to give his undivided attention to the treatment.—I am, etc.,

Manchester. M. D. MILNE.

Normal Clotting Time

SIR,—In his interesting article on intramuscular heparin (December 23, 1950, p. 1418) Dr. D. Gordon Abrahams says that the normal clotting time determined with the Dale and Laidlaw technique is 2½–3 min. In fact the normal time by this method is pretty constant at 1 min. 40 secs., and any reading over 2 min. should be considered raised. This point may be important in accurate treatment with heparin.—I am, etc.,

Canterbury. I. B. MORRIS.

Neuromuscular Relaxation

SIR,—Your annotation (January 20, p. 132) on a new muscle relaxant, mephenesin, in which you point out that this drug has been found to produce "increased fragility of the erythrocytes, possibly resulting in dangerous anaemia," and yet suggest that it may be of use in the treatment of psychiatric cases characterized by excessive tension, prompts me to urge the practice of intensive suggestion treatment with controlled breathing as a preferable, more effective, and safer method of bringing about a reduction of neuromuscular tension. Deep breathing, *with a pause of one or two seconds after expiration*, helped out by strong suggestions of sleep and of mental and muscular relaxation, can be effective in a large proportion of nerve cases, and in only a small minority are drugs necessary. I call this the method of the "post-expiratory pause," and have proved its effectiveness in many years of practice. The pause probably facilitates the spread of relaxation from the voluntary muscles to the involuntary muscles (of the blood vessels, bronchioles, and digestive tract, etc.) and on to the autonomic nervous system controlling the latter. Analytical

psychotherapy, involving the relief of repressions through emotional abreaction and the production of deeper insight by the patient into his mental condition and its causes (autognosis), acts in the same direction and should also be applied where possible. But direct suggestion, etc., may often be very effective in procuring for the patient the rest and the neuromuscular relaxation which is needed as a preliminary to more radical treatment and cure.—I am, etc.,

London, W.1. WILLIAM BROWN.

Skin Disease and Psychology

SIR,—The numerous claims of psychological medicine over the whole gamut of human ills, from criminal and sexual disorders right through to organic disease, have on the whole been singularly free from criticism in our journals (although among our colleagues one finds a more vigorous and robust outlook). Now, however, one hopes that the Linacre lecture by Dr. F. M. R. Walshe (August 12, 1950, p. 379), with the rather amusing psychiatric reaction to it in your correspondence columns, may be the long-awaited lead needed to stimulate us to re-examine these claims and by doing so rid ourselves of a great deal of mumbo-jumbo which has gone unchallenged as scientific thought during the last thirty years. May I therefore, humbly following such a lead, "abreact" to the recent article by Shorvon and his co-workers[1] on the psychological treatment of skin diseases?

To criticize this communication, one must admit at the outset, is difficult, not because one is struck by the truth of the thesis, but merely through the fact that it claims so much and yet so little, as is indicated by this pathetic sentence in the discussion, "Although we do not claim that this method is the only one that may be employed, or that all cases are cured or benefited by it, we have found it of definite value in a considerable proportion of all cases considered to require treatment by a psychiatrist." However, in spite of the difficulties, let me put a few points for consideration.

Type of Case Treated.—It will be noted that the cases chosen are those diseases whose aetiology, many believe, is as yet shrouded in mystery; and, although a psychological cause has occasionally been suggested, this has not made their origin less obscure. Let us discuss acne rosacea. Sneddon[2] suggested, and this suggestion has been eagerly seized upon by the psychiatrists, that it arises from a suppressed sense of shame, which by causing subnormal blushing over a period of time leads to chronic dilatation of the blood vessels and so eventually to the fully developed clinical picture. Certainly an attractive theory, but unfortunately the disease is sited centrally on the face and forehead, while blushing is a physiological reaction which spreads centripetally from the neck and behind the ears, leaving the central part of the face free, often in vivid contrast to the blushing areas. (Even the poets knew this.) On the other hand, the distribution of the disease on the central part of the face is not without its counterpart in organic disease, since the well-known post-encephalitic seborrhoeic syndrome affects the same area, and, although the reference is lost to me at the moment, it has been found that there is a distinct physiological difference, as shown by electrical resistance studies, between this area and the more peripheral areas of the face. These facts indicate that the distribution, far from being psychologically determined by suppressed blushing, has its roots in physiological and pathological processes as yet imperfectly understood.

To discuss, however briefly, such conditions as lichen planus, psoriasis, and, yes, even pruritus ani and vulvae would unnecessarily lengthen this letter, but I feel that most of my colleagues would agree that from our present knowledge of these diseases and their clinical characteristics a psychological basis is the funkhole of scientific investigation.

Results of Treatment.—It is in the experience of all dermatologists that in the diseases listed improvement and often complete disappearance of the lesions and symptoms frequently occur after the most varied empirical approach, but we are too wily to contend that these methods have anything to do with the observed results. We accept the good results gratefully, knowing from our experience how disappointed we are going to be when we find that our earlier successes are not subsequently maintained. May I give details of a case in my own experience? A man had a widespread eczematous excoriated eruption affecting the whole skin surface, and in spite of the appalling condition of his skin he seemed to be on the whole relatively unconscious of its severity. He was admitted to hospital and with rest in bed, coupled with bland applications, he settled down and was discharged. When seen again some months later it was learned that he had relapsed after leaving hospital, and that in the interim a leucotomy had been performed. After the operation it appears that his skin cleared satisfactorily, but, unfortunately for cause and effect, his skin again relapsed, and on this occasion he cleared on Lassar's paste with crude coal tar. Comment is, I think, unnecessary.

The Abreactive Technique.—At first sight this gives one the impression of something new, but, in the words of the authors, it is "getting things off one's chest, especially when accompanied by varying degrees of emotional reaction." That this is true is within the experience of all, and the only difference with the present method is that a drug is added, but how far the emotional response noted during the abreaction is due to the content of the mind at the time and how much to the pharmacological effects of the drug one has no way of telling. It will be observed, however, in reviewing the cases, that surprising emotional effects accompany episodes of a trivial nature while little occurs after seemingly severe psychological trauma, and furthermore that some of the events accompanied by emotion occur long after the lesions appear.

Finally, one is left with the impression that a series of cases of skin disorders of unknown aetiology were treated by various drugs for no earthly reason except that a psychological cause had on occasion been suggested, and that these disorders improved in some cases while others of apparently the same type showed no change. When added to this we recall the further fact detailed in this letter, that these diseases react to various empirical methods in exactly the same way, our conclusion must be that the abreactive technique in the treatment of these disorders has no claim whatsoever to be added to our armamentarium, since the same result can be obtained by methods which vary from colourful applications to the parts to murmuring incantations while burying legendary herbs during the period of the full moon.—I am, etc.,

London, W.1. F. L. LYDON.

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2 Sneddon, I. B. (1949). Ibid., 1, 472.

Skin Pigment and T.B.

SIR,—Dr. J. N. Briggs and his colleagues (January 20, p. 115), in describing Addison's disease in two brothers, suggest the possibility that a genetic factor may be involved in the occurrence of the disease. This recalls to memory the case of a young man who when recovering from tuberculosis of the bones of the foot was noted to have developed pigmentation of the skin. He became greatly perturbed when he was asked to strip for a closer examination, and explained that he was well acquainted with the condition, as his father had died of it, although so far as he was aware his parent did not suffer from any obvious tuberculous lesion.—I am, etc.,

Ross-shire. J. LANDESS HORNE.

Treatment of Lumbar Disk Lesions

SIR,—In his recent article (December 23, 1950, p. 1434) Dr. J. Cyriax gives a lucid account of the methods he employs so successfully in the treatment of lumbar disk lesions. It is, therefore, a pity that he gives so little credit to other methods employed with equal success by other practitioners. Many disk lesions, especially when complicated by sciatic pain, do not respond to manipulation, traction, epidural injection, or to Dr. Cyriax's only other alternative, bed rest. Bed rest is seldom complete, owing to the daily bed-making and the calls of Nature, and these are the cases which the more conservative of us treat by immobilization in a plaster-jacket, relief of symptoms usually being rapid and permanent, provided the jacket is worn for a sufficiently long period. Though there may be some temporary initial discomfort, a well-padded and moulded plaster

soon becomes so comfortable that the patient almost forgets he has got it on.

It is perhaps because he does not believe that disk lesions are capable of repair that Dr. Cyriax has so little use for plaster jackets. Because the annulus is avascular it does not necessarily imply that repair by scar tissue cannot take place. M. B. Coventry, R. K. Ghormley, and J. W. Kernohan (*J. Bone Jt Surg.*, 1945, 27, 460) in their study of lumbo-sacral disks removed at necropsy observed fissures in the annulus being canalized by blood vessels from the spongiosa of the adjacent vertebrae—Nature's method of repair.

Dr. Cyriax's classification of disk lesions into cartilaginous and pulpy protrusions, while highly ingenious, hardly gives a complete picture of what may happen when a disk sustains trauma. It is difficult to understand how a pulpy protrusion can occur with an intact annulus. Surely if the annulus has become detached from the rim of the vertebra it can no longer be intact. Again, not all pulpy protrusions are marginal. At operation the surgeon has often demonstrated to me a postero-lateral bulge, midway between the vertebral bodies, the essential lesion being a partial tear leading to a weakening of the annulus, the bulge being secondary to the tension of the nucleus.

Now that we have all become disk-minded there is a tendency to forget the other components of the intervertebral joint, and I am sure that in many cases of chronic low backache the pain arises in the ligamentum flavum. M. B. Dockerty and J. G. Love, of the Mayo Clinic (*Proc. Mayo Clin.*, 1940, 15, 161), stress the fact that the ligamentum flavum frequently sustains trauma concurrently with the disk. The ligament becomes thickened, the elastic fibres being replaced by fibrous tissue. They term the condition "hypertrophy with fibrosis." It may well be that this type of case would respond to sustained traction as described by Dr. Cyriax. Possibly also, in view of the fact that the disk is not the only component of the intervertebral joint, "deranged intervertebral joint" would be a more suitable form of diagnosis.

Finally, although I am afraid Dr. Cyriax will not agree, there still is a place for short-wave diathermy and massage in the treatment of disk lesions. Short-wave diathermy by its deep-heating effect can bring some relief to the pain caused by the inflammatory reaction at the site of the lesion. Likewise light massage in skilful hands can do much to reduce muscle spasm.

—I am, etc.,

London, W.1. E. J. CRISP.

Pethidine Sensitivity

SIR,—Dr. D. Zuck's description (January 20, p. 125) of his case of pethidine sensitivity is not altogether convincing. Can he genuinely attribute the adverse symptoms described solely to the administration of pethidine when a variety of different drugs were being used? It is by no means uncommon to see a sudden and severe rise in the pulse rate following the administration of "flaxedil" with any combination of anaesthetics. I would agree that nitrous oxide and oxygen with pethidine and a suitable muscle relaxant can provide "perfect operating conditions," but in an unselected series of nearly 500 cases I have seen no single instance in which pethidine *per se* has caused any ill effect.

—I am, etc.,

Folkestone. HARRY F. GRIFFITHS.

SIR,—Dr. D. Zuck's report of a case of pethidine sensitivity (January 20, p. 125) prompts me to record a similar case.

The patient was a woman aged 62 years, of average size and good general health, blood pressure 160/100 mm. Hg. The operation was for the repair of a second-degree vaginal prolapse. Premedication was ¼ gr. (10 mg.) morphine and 1/100 gr. (0.6 mg.) atropine given 60 min. pre-operatively.

Anaesthesia was induced with 0.4 g. thiopentone and continued with nitrous oxide with 25% oxygen, administered by a Boyle's machine. Five minutes after induction, as anaesthesia was still very light, and after the patient had been placed in the lithotomy position, a further 0.2 g. thiopentone was given. Anaesthesia was now evenly established, and 25 mg. pethidine was given into a vein on the dorsum of the hand. The patient became apnoeic within a very short space of time, and was inflated rhythmically by manual compression of the rebreathing bag. Nitrous oxide with 25% oxygen was given throughout. After five minutes, respiratory arrest was replaced by isolated deep respirations at the rate of two per minute. Fifteen minutes after the dose of pethidine had been given the respiratory rate was three per minute, the blood pressure was 100/60 mm. Hg, and the patient's colour and capillary refill time were good. After a further five minutes the blood pressure had fallen to 90/60 mm. Hg and it did not rise above this level before the end of the operation.

The operation lasted for 55 minutes. During the posterior colpoperineorrhaphy anaesthesia was very light and the patient began to move her legs. A dose of 0.15 g. thiopentone was given and this sufficed for the remainder of the operation. The respiratory rate was seven per minute when the patient was returned to bed. Oxygen was then given by nasal catheter at a flow of 7 litres per minute.

Recovery from anaesthesia lasted one hour. The patient was then fully conscious. Her blood pressure had gone up to 130/80 mm. Hg and her respiratory rate to 12 per minute. She did not complain of any pain. One hour later the respiratory rate was 15 per minute and the blood pressure 140/85 mm. Hg. In the post-operative period an intradermal injection of 0.1 ml. pethidine solution was followed by the development of a weal 1 in. in diameter and surrounded by an area of hyperaemia. A control injection of normal saline proved negative.

I am indebted to Mr. G. Millington for permission to publish this case and to Dr. M. Swerdlow for his advice.

—I am, etc.,

Warrington. M. D. FIELDING.

Smallpox and Human Sacrifice

SIR,—Dr. I. C. Monro in his letter (January 20, p. 136) states: "The tragedy is that not one of these deaths is necessary. . . . Deaths from smallpox very seldom occur after successful infant vaccination." He goes on to refer to the "gross negligence of parents who omit to have their children vaccinated in the first year of life. If this practice was universally carried out it would take only a few years to build up the community's resistance so that death from smallpox became impossible."

One can only think that Dr. Monro has not had much experience of smallpox, and is not familiar with the literature of the subject, or he would not have ventured to make an assertion so greatly at variance with the truth. In almost every outbreak of smallpox a substantial proportion of the fatal cases occur among persons who have been vaccinated in infancy. It so happens that I have just been re-reading the official report on the outbreak of smallpox which occurred in Edinburgh (originating in the Royal Infirmary) in 1942. If Dr. Monro will look up page 32, Table VI, of that report he will see that of 18 vaccinated patients no fewer than six died, five of these being haemorrhagic. I admit that the figures were rather exceptional (as well as being very small), because among nine unvaccinated cases there happened to be only two deaths; but with these figures before him I think that Dr. Monro must admit that his assertion was, to say the least of it, "wildly beside the mark." If it is any comfort to him he will also see that among nine revaccinated cases there were no deaths.—I am, etc.,

Leicester. C. KILLICK MILLARD.

Health, Diet, Soil

SIR,—I was glad to see Dr. Jordan's letter on this subject in the *Journal* (January 20, p. 137). I, too, wonder why so little attention has been paid to the factor of diet in disease production and prevention. It appears to me that the work of Sir Robert McCarrison in the field of preventive medicine has been lost in the maze of hyperspecialism, where none can see the wood for the trees. It was McCarrison, not Howard, who first drew attention to the wonderful effects of the diet of the northern tribes of India in his Cantor Lectures. He says. "So impressed was I by the adequacy of the northern Indian's diet that during the later years of my experimental work I used it as the diet of my stock rats. These numbered about 1,000. . . . During the five years prior to my leaving India there was in this stock no case of illness, no death from natural causes, no maternal mortality, no infantile mortality. It is true that the hygienic conditions under which they lived were ideal. . . . But the same care was bestowed during these years on several thousand

deficiently fed rats, which developed a wide variety of ailments, while the well-fed animals enjoyed a remarkable freedom from disease. It is clear, therefore, that it was to their food that this freedom was due." Surely this was an amazing achievement in preventive medicine, yet it has been lost sight of by the bulk of the medical profession.

As Dr. Jordan points out, Howard, in the agricultural world, stressed the importance of growing food crops on organic principles, and claimed that by his methods of feeding and husbandry the natural resistance to disease of his stock was raised to such an extent that they did not contract foot-and-mouth disease when exposed to it. If this is correct it is a most important step forward from McCarrison's experiment, as I doubt whether McCarrison's stock rats were ever purposely exposed to acute infectious disease.

I think that it is of the utmost importance that the comparative immunity to foot-and-mouth disease and other diseases of organically raised and other stock should be tested by exposure to those diseases. Recently I had the privilege of visiting the farm of Mr. Friend Sykes, at Chute, along with a number of medical friends. Mr. Sykes also claims to have banished disease from his stock by his methods of organic farming. We were all very much impressed by what we saw, and by Mr. Sykes's answers to our questions. I suggest that the Medical Research Council should sponsor (1) an investigation such as I have outlined above, (2) an examination of Mr. Sykes's records of the past 15 years, and (3) an examination of the results of the long-term investigation of this subject undertaken by the Soil Association on their farm at Haughley. If this were done I believe it would result in a complete vindication of McCarrison's statement that "the greatest single factor in the acquisition and maintenance of good health is perfectly constituted food."—I am, etc.,

St. Mawes, Cornwall. N. C. PENROSE.

Metabolic Effects of Salicylate

SIR,—Your correspondent, Dr. S. W. Stansbury (January 20, p. 138), assumes that in our paper (Reid, Watson, Sproull, 1950, *Quart. J. Med.*, n.s. **19**, 1) we consider the reaction change in rheumatic fever resulting from salicylate administration is a "primary" respiratory alkalosis. This is not correct. We did not qualify the term respiratory alkalosis in our paper, for two good reasons. First, our findings would not permit more detailed description, as the rise in plasma *p*H and fall in plasma CO_2 content developed simultaneously in both patients. Secondly, though a primary respiratory alkalosis may be conjectured it is difficult to reconcile this with the fact that hyperventilation from salicylate subsides, and the plasma *p*H actually falls, when sodium bicarbonate is given. We thus consider that the origin of the reaction change to salicylate in rheumatic fever remains a puzzle and so cannot accept Dr. Stansbury's interpretations of our findings.

I thank your other correspondent, Dr. Paul (January 20, p. 139), for his interesting comments on the reducing substances which may appear in the urine during salicylate treatment.—I am, etc.,

Glasgow. JAMES REID.

"A Kick in the Pants"

SIR,—The departure of Mr. Aneurin Bevan from the medical scene was an event which called for a fuller notice in the *British Medical Journal*. Omitted were the facts that the Right Honourable gentleman had held office as Minister of Health longer than any of his predecessors and that, the electorate having expressed the wish in 1945 for a National Health Service, he undertook the most onerous task that has yet befallen a Minister of Health. No offence will have been taken by having mentioned that the B.M.A. disagreed with many of his numerous and difficult decisions, but it would have been courteous at least to wish him well in the new and heavy responsibilities which he has been called upon to accept.

The pity is that a professional journal, when bidding a statesman farewell from the medico-political arena, disregarded his sterling qualities and denigrated his ability. I can only surmise that the *B.M.J.* was influenced by the feeling of the Opposition. May I ask whether it is in keeping with medical tradition for the *B.M.J.* to undertake a function of the Tory press? Is it really too much to expect that the B.M.A. should, regardless of whichever political party holds power or whoever may be Minister of Health, show itself the essence of professional decorum and refrain from giving a vulgar "kick in the pants" to one of His Majesty's Ministers? Has the time not yet arrived for the B.M.A. to cease being a puppet of the Conservative Party and to return to its stand as a professional organization removed from party politics?—I am, etc.,

London, S.W.1. A. D. D. BROUGHTON.

Fate of a Good Samaritan in Burma

SIR,—I hope that the medical profession in this country will not accept without uttering a protest the sentence of six years' imprisonment recently passed by a Burmese court on Dr. Seagrave. Here, more important issues are involved than local Burmese politics. A doctor must be allowed to work outside the noisy ring of politics and to administer to the sick irrespective of their party. He must refuse to aid only those of which the Government in power happens to approve. The charges brought by the Burmese authorities against the Western doctor who had done such excellent work in their country were utterly trivial: that when the Kachin insurgents captured the town in which he was working he was polite to the commanders and even offered them tea; that he allowed them to take away certain medical supplies which they badly needed. The fact that he was their prisoner and had no power to restrain them does not seem to have been taken into account. In any case six years' imprisonment does not appear to be a suitable sentence for being amiable and polite to one's captors. The utmost publicity must be given to this case. Although the rulers of Burma have elected to be politically independent of the Commonwealth, economically Burma is not self-sufficient and cannot, therefore, afford to affront Western codes of behaviour. It is to be hoped that some international medical body will take this case up. Dr. Seagrave not only worked as a doctor, but set up in Burma an organization for the training of the nurses which that country so badly needed. He was therefore a representative of international medicine and can claim the help of any medical or health organization working on a world scale.—I am, etc.,

London, W.1. KENNETH WALKER.

POINTS FROM LETTERS

Registrar Appointments

Dr. JOHN FORBES (Adwy, near Wrexham) writes: . . . [There] is the difficulty that senior registrars in non-teaching hospitals have in obtaining consultant posts when they are in competition with senior registrars from teaching hospitals. Similarly, non-teaching hospital registrars are at a disadvantage when it comes to getting senior registrar posts in a teaching hospital against the competition of registrars from that hospital itself or from other teaching hospitals. . . . I would like, therefore, to put forward a practical proposal—namely, that in the future senior registrar posts should be largely confined to teaching hospitals, whereas registrar posts should be largely confined to non-teaching hospitals. This would mean that a trainee would after finishing his senior house-officer appointments be more or less compelled to continue his apprenticeship as a registrar at a non-teaching hospital. After two years, however, he would be able to apply for a senior registrar post at a teaching hospital, where his training would be completed. In this application he would be competing on equal terms with registrars from other non-teaching hospitals

Influenza

Dr. W. L. FRAZIER (Los Angeles, Calif.) writes: . . . I used colloidal silver intravenously in combating the type of influenza epidemic in 1918–19, and I am convinced it is specific for that type. . . .

Obituary

SIDNEY P. PHILLIPS, M.D., F.R.C.P.

The death on January 19 of Dr. Sidney Phillips, in his 100th year, at St. Mary's Hospital after an illness of only a few days will be greatly regretted by all who knew him. He was second senior Fellow of the Royal College of Physicians of London, where he was Treasurer for 14 years, from 1924 to 1938. Though he outlived nearly all his contemporaries, and very few at St. Mary's Hospital remember him, numbers of his former pupils still in practice will remember with gratitude his tutorial classes in medicine. For the past ten years his total blindness from chronic retinal degeneration had restricted his activities greatly, so that he lived most of the day in his armchair in Park Chambers, Queen's Gardens, not far from the hospital where he spent a large part of his working life.

We are indebted to Dr. Wilfred Harris for the following appreciation: Sidney Philip Phillips was born on July 27, 1851, at the time of the Great Exhibition in Hyde Park, and we all counted on his reaching his century, for his mind and memory were so clear, and he thoroughly enjoyed talking over old times. His father was in business in the City, but died in early middle life before Phillips was qualified. Phillips then set out to keep himself by coaching and so spare expense to his mother, who had three other children. He was fond of climbing, and he held a certificate of having ascended Mont Blanc in 1871 when aged only 20. Like other men and women of his generation he saw great changes. St. Mary's was just built and was opened to patients in the year he was born. As a boy he used to fish not far from his home in Queen's Gardens in the West Bourne, a stream which ran down Craven Terrace on its way to the head of the Serpentine, just inside Kensington Gardens. He was educated at University College School, then housed in the south wing of University College, and, since he disliked the idea of business and wanted to become a doctor, it was natural for him to proceed to University College and its medical school. The new University College Hospital, since built by Sir Blundell Maple's generosity, was then scarcely thought of. In the old building—famous for men like Sir William Jenner—Phillips, after qualifying in 1877 and gaining the gold medal for materia medica and therapy, served as house-surgeon, house-physician, ophthalmic assistant, and junior demonstrator of anatomy. He had graduated M.B. in 1878, and proceeded M.D. two years later. As no opening seemed possible just then at University College he applied for the post of medical registrar at the Middlesex Hospital, which was also advertising for a surgical registrar. When interviewed by the committee he was asked whether he intended to devote all his time to medicine in the future; he answered "Yes," but was turned down. So he hurriedly applied for the surgical post, and half an hour later was asked by the same committee whether he intended to devote his whole time to surgery. Again he answered "Yes," and got the appointment. This story he told me years ago, as a great jest. He served the Middlesex for two years, from 1880 to 1881, living then at 12, Radnor Place, near St. Mary's, so it seemed natural that he should apply for a post there, being appointed in 1881 as senior demonstrator of anatomy, a post he held for four years. In 1883, the year he became a Member of the Royal College of Physicians, he was appointed assistant in the medical out-patient department, and in the following year physician to out-patients, becoming full physician in 1896 on the retirement of Sir William Broadbent.

Perhaps Phillips was best known at St. Mary's for his ward classes as medical tutor, which he carried on from 1890 to 1901, after he was promoted to the full staff. He had a good-natured, pawky humour, and was fond of teasing his students in class by laying simple traps, such as telling them to listen to an inaudible heart in a man with gross emphysema and then questioning them on what they heard. In those days at the annual hospital dinner Phillips and Edmund Owen were always put up for a speech, and many a quip would be bandied between them. Herbert Page was another orator we generally heard. *O si sic tempora!*

About the time Phillips became physician to out-patients he was also appointed to the London Fever Hospital in the Liverpool Road, to the Lock Hospital, and to the Paddington Green Hospital for Children. In 1891 he was elected F.R.C.P. From the autumn of 1914 until April, 1919, he served as lieutenant-colonel in the R.A.M.C. (later becoming brevet colonel) at the 3rd London General Hospital, Wandsworth, on the medical side, the hospital being run jointly between the Middlesex, University College, and St Mary's. At the same time he served as a special constable for four years, so that his health failed somewhat towards the end of the war, and he suffered badly for months from boils, enduring many treatments from tin to vaccines. In 1920 he retired from St. Mary's, becoming consulting physician. Besides being treasurer, Phillips was also an examiner to the Royal College of Physicians, as well as to the University of London and the Society of Apothecaries. At one time he was president of the Harveian Society. He published numerous papers, mainly on fevers and diseases of the heart and organs of digestion. For five years of the late war he lived in the country near Churt, but in 1945 he returned to London. For the last 14 years of his life he was looked after by his devoted nurse, Miss Doyle. He was a member of the Bath Club for many years, and also of the Savile Club when housed in Piccadilly. Phillips never married. In appearance he was tall and thin, with aquiline features, iron-grey hair and a clipped moustache.

WALTER WALKER PALMER, M.D.

We record with regret the death of Dr. Walter W. Palmer, of New York, on October 28, 1950. For the following appreciation we are indebted to Professor J. W. McNee.

Dr. Walter Walker Palmer, always known as "Bill" Palmer to his host of friends in the United States and to many physicians in Britain and Europe, died last October at his country home in the lovely Tyringham Valley, Mass., from coronary disease, aged 68 years. The news has only recently filtered through to Britain, and there is an obituary notice in the *Journal of the American Medical Association* of December 23, 1950, describing briefly the many facets of his distinguished career as physician, teacher, and administrator. Bill Palmer was one of the best-loved medical men in America, and for 26 years (1921–47) was Bard Professor of Medicine at Columbia, New York, and director of the medical service at the Presbyterian Hospital. He had much to do with the transfer of this hospital from

its old building down-town to its new palatial premises far up-town. He retired from his chair in 1947, and was succeeded by Dr. Robert Loeb. This, however, simply meant a transfer to another important post, and he moved down-town again to direct the new Public Health Research Institute of New York.

A medical graduate of Harvard in 1910, Palmer's first opportunity came with his appointment to the Rockefeller Hospital, New York, in 1915. Thereafter he spent two years (1919–21) as associate professor of medicine at Johns Hopkins, Baltimore, before returning to New York, where most of his active life was spent. His best-known research work was on acid-base equilibrium (with L. J. Henderson), and his other main interests were in diabetes and thyroid disease. Palmer at one time or another was president of most of the chief medical societies in the U.S.A., including the Association of American Physicians and the New York Academy of Medicine. He served in the first world war, and thereafter gave expert assistance to many Government departments.

Bill Palmer was a big, burly man of great charm and with the heart of a boy. The writer visited him in New York in the autumn of 1949, and also spent a happy day with him in company with Professor Warfield T. Longcope at the farm in Massachusetts. There Palmer enjoyed to the full his holiday hobby of making beautiful furniture; his workshop, filled with shining electrically driven saws, planes, and lathes, was his great pride. Palmer was certainly one of the really big men of American medicine in his time, and will be greatly missed.

GASTON COTTE, M.D.

Professor Gaston Cotte, who has recently died at the age of 71, was one of those fortunate surgeons who, by the invention of an original operation which has stood the test of countless successful performances, have achieved lasting memory. Presacral neurectomy has proved one of the most beneficial of sympathetic-system operations, and, though independently discovered and largely popularized in this country and the United States by Davis, credit for precedence must remain with Cotte, whose papers anteceded those of Davis by several years, though obscured by their publication in a journal of somewhat limited circulation—*Lyon Médical*. His book, *Chirurgie du Sympathique Pelvien en Gynécologie*, was published in Paris in 1932.

A native of Lyons, Cotte remained faithful to that city throughout his life, and, with the exception of three years spent as surgical specialist at Salonika, passed the whole of his professional career there, eventually succeeding his teacher, Pollosson, as professor of clinical gynaecology. He had always been interested in the problem of gynaecological pain, and, with Leriche carrying on his pioneer work in the neighbouring clinic, sought through sympathectomy of various types to produce the desired effect. But it was largely due to the newer anatomical concepts enunciated by another Lyonnais, Latarjet, that he was able to point the way to rational nerve division, and to show that there was an easily accessible nerve bundle—the presacral nerve—division of which would cut off effectively the entire abdominal sympathetic supply to the uterus. It was not long before the operation of presacral sympathectomy was universally adopted, at first with somewhat uncritical enthusiasm, but it has weathered the test of nearly 20 years, and remains of curative value in cases of intractable dysmenorrhoea and an indispensable adjunct to operations for painful pelvic conditions such as endometriosis.

The gynaecological clinic at the Hôpital Grange-Blanche became the Mecca of surgeons and gynaecologists throughout the world, with Cotte ever ready and eager to welcome and demonstrate. Yet withal, and in spite of multiple honours, including the British D.S.O., the Legion of Honour, and the presidency of the Lyons branch of the Red Cross and of the Lyons Medical Society, he remained the most modest of men. His charm and boyish enthusiasm remained to the end, and his passing deprives the profession of a distinguished and lovable personality.

G. E. GASK, C.M.G., D.S.O., F.R.C.S.

Professor G. Grey Turner writes: From just after the 1914–18 war Professor Gask was very interested in the idea of the development of a postgraduate medical school in London. He was untiring in his efforts, and devoted much thought and time as well as work on committees to further that end. When the idea took shape he was appointed by the senate of the University of London as one of the representatives on the Governing Body and was later the first chairman of the School Council, a position he filled with great assiduity. Gask always hoped that one of the well-recognized teaching schools would be willing and perhaps even eager to switch over from undergraduate to postgraduate activities, but when that did not come to fruition he adopted the proposal to adapt one of the L.C.C. hospitals, and did his very best to help the development of the Postgraduate School in Ducane Road. He certainly did a great deal to guide the destinies of the new venture in the early years, and often against opposition from more than one quarter. Having once convinced himself on what was a proper course Gask was not easily deterred. He was a man of big ideas, but it was more his *forte* to initiate and guide than to work out details. To him it was almost a knock-out blow when on account of the financial crisis of 1931 it was necessary for the Treasury to cut the proposed grant by half, and he always felt that the venture was crippled from the outset to that extent. But he carried on and tried to establish those ideas which he had nourished, encouraging here and stimulating there, and doing what he could to build it up. Of course there were those who predicted that the scheme was doomed to failure, and his faith and determination and quiet persistence were great assets in those early days. Gask took great pains to select what he considered the proper people for the various posts, but once they were installed he believed they should have their head and was prepared to make great allowances until they could prove themselves. There was no premature fussy interference. He was most keen on the importance of records, and it was one of his favourite ideas to set up a master scheme that might form a model of something really worth while, but there were many frustrations.

There was another characteristic to which I would like to refer. Towards the end of the 1914–18 war Gask and I were in New York together on a War Office mission, when news of the armistice came through. Up till that time I had always regarded Gask as one of those big silent men without a touch of sentiment, but I can never forget the deep emotion which he showed on that occasion. Perhaps the emotional surge even took him by surprise, for to explain his tears he told me he was thinking of dead

boys on the battlefields of France. Gask really loved the young and unobtrusively spent his life in trying to guide and help them. In many ways Gask was a great fellow, whom it was a privilege to have known so intimately.

Sir ARTHUR HALL, M.D., F.R.C.P.

C. W. B. writes: May I, as an admirer of the late Sir Arthur Hall from the day, 60 years ago, when in friendliest fashion he came to the help of a raw first-year student, working at his first "part" in the dissecting room in Leopold Street, Sheffield, express appreciation and thanks for the obituary notice in the *Journal* of January 20 (p. 140), with its record of Sir Arthur's great achievements for the city of Sheffield and for the profession which he adorned? One found in his helpfulness and patience with minds less well-equipped than his own a powerful attraction, whether one was acting as practical physiology or clinical clerk or playing next to him in the school orchestra, or in later years as his patient. A. G. Y. speaks very truly for those who have lost in him a generous and charming friend. Now he has joined "the choir invisible of those immortal dead who live again in minds made better by their presence."

Dr. WILLIAM BENTON, for many years medical officer of health of East Ham, died at Thornton Heath, Surrey, on December 5 at the age of 82. Born at Barrow-on-Soar, Leicestershire, he went to Barrow Grammar School, and studied medicine at Charing Cross Hospital, qualifying in 1896. After holding a resident appointment as obstetric house-physician at Charing Cross Hospital, he served for a short period as ship surgeon, and then settled down at Upton Park, London, in 1898 in general practice. In 1903 he obtained the D.P.H., and in 1909 he was appointed deputy M.O.H. to the County Borough of East Ham in a part-time capacity. Eighteen months later he gave up general practice on his appointment as M.O.H.—a striking testimony to the confidence and affection his devotion to his patients had inspired in the borough. His new duties included charge of the isolation hospital. But his experience of general practice was not wasted: it made him realize the need for the school medical services which he initiated, and inspired his pioneer activities in maternity and child-welfare clinics. The first municipal baby clinic was inaugurated in 1912; it was on a voluntary basis at first, but in 1914 it became a full function of the council. In the 1914–18 war he served as a lieutenant in the R.A.M.C. and was assigned duties in examining recruits and as battalion M.O. He took a great interest in the St. John Ambulance Brigade, being a divisional surgeon and examiner; he was decorated with the Order of St. John, and in 1948 was presented with the insignia of a Commander, an honour which gave him great pleasure. He was examiner for the General Nursing Council of England and Wales, and a past-president of the Home Counties Branch of the Society of Medical Officers of Health. East Ham was not ungrateful for his services. He was a past-president of its Rotary Club, and on his retirement in 1935 he was given the freedom of the borough and made a J.P. In 1936 he retired to Worthing, but not to idleness. From 1938 to 1946 he was a member of the town council, becoming chairman of the public health committee. He also retained his appointment as examiner for the Southern Railway, and continued his ambulance work as divisional surgeon to the Lancing and Sompting Division. Benton was a member of Gray's Inn and a Freeman of the City of London. His wife died in 1939, and his two sons, both members of the medical profession, survive him. He leaves the priceless memory of a long career of eager and unselfish service based on Christian ideals. The writer mourns the end of an unclouded friendship of sixty years.—W. S. H.

Medical Notes in Parliament

Pensions for Disabled Men

On January 23 Mr. LESLIE HALE raised the subject of pensions for disabled persons. He said that in his division he had been confronted time after time with cases of disseminated sclerosis and Parkinsonism. A man who had joined the Forces officially fit but came out crippled by the disease was unable to establish that it was due to service in the Forces, because no one knew the cause of the disease. There was no known medical origin, and it was therefore utterly impossible for any man before the Medical Appeals Tribunal to establish affirmatively that his disease was caused by war service. Mr. Hale suggested that in such cases the burden of proof ought to be shifted. Some decisions by Mr. Justice Denning certainly seemed to shift it, but there had been no attempt by the Medical Appeals Tribunal to consider the matter purely on medical grounds.

Turning to the general question of pensions for disabled men, Mr. Hale said that the policy of the Government had been quite rightly to regard the very serious totally unemployable cases as peculiarly worthy of special care. He thought, however, that too small a percentage of pensioners were receiving the additional allowances. Out of a total of 600,000 about 6,000 pensioners received an unemployability supplement, about 8,000 had a compensating pension for diminution of occupational capacity, and less than 3,000 received a constant attendance allowance. There would be great satisfaction if the criteria of unemployability were applied a little less rigidly. He felt that more might be done to provide work in the home, and he was distressed by the number of people who were employable but who, because of their medical record, failed to obtain employment. The nationalized industries had not a good record in this respect. Work should be found for these people, because the amelioration of their sufferings lay in work.

Medical Attitude to Claimants

Mr. Hale said he was worried about the attitude sometimes shown towards chronic sufferers. He knew of one man who had in his records, "He limps, and will continue to limp so long as he gets money from the R.A. Corps, from the National Health, and the Ministry of Pensions," and yet there was no doubt about the genuineness of this man's case.

Another man suffered from bilateral otitis media during his service in the Army. He was discharged and given a fair pension, and then went before a Medical Survey Board, who examined him and reported that his general condition was good. Five weeks later he died, and the post-mortem examination revealed the cause of death as due to myocardial degeneration and arteriosclerotic nephritis. He said that, if a Medical Survey Board examined him to-day and in five weeks' time he would be dead with something seriously wrong with his heart and arteries, then he lost faith altogether in medical examinations. In this case a wretched dispute followed with the Appeals Board about whether this man's death could have been caused by otitis media. Most textbooks said that nephritis frequently followed otitis media. Mr. Hale thought that in a case like that it would be reasonable for the Ministry of Pensions to say that, as the man had been gravely ill in the Forces, had been ill ever since, and had died prematurely, the case was one where there should be a pension.

There were other cases he knew of which were also worrying. One Oldham man who served in the 1914–18 war said he had been shot in the shoulder, and went on saying it. After 30 years he was still told that this was not so and there was nothing to complain about, but when he was finally radiographed in Oldham Infirmary a bullet was discovered and taken out. The Ministry had then given

him a pension, but refused to pay back-money, although the man had been claiming every two or three years since 1918.

Mr. E. A. A. SHACKLETON quoted cases where a more sympathetic approach to the employment of disabled men was needed. He also mentioned that many parents whose sons were disabled felt deeply that their own plight should be recognized and that there should be a more generous judgment of their need as dependants in awarding pensions.

Dr. CHARLES HILL said that though it might be impossible to prove that service caused disablement, if no one knew the cause then no one could exclude the factor of service. He commented on the number of out-of-date motor-propelled invalid tricycles, for which maintenance was difficult, and he asked that the new models should have a reversing gear and, if possible, a seat for a companion so that the invalid need not go out in solitude.

Influence of Medical Opinion

Mr. R. V. MELLISH said that Pension Appeals Tribunals were often confronted with a *fait accompli* before the cases had been heard, because of the medical opinion. Medical opinion, for instance, said that diabetes mellitus was, in the main, hereditary and that conditions of hardship were not necessarily contributory. Likewise with disseminated sclerosis, they held that it was in the main hereditary and therefore nothing to do with the man's service in the Forces.

Mr. BASIL NIELD said he hoped that in future it would be a matter for the Ministry to show that the disability did not arise from service rather than a matter for the disabled person to establish that it did. He remarked that it was often impossible to convince an unfortunate person that his service had nothing to do with the disability, whatever the doctors said, and since a man might in any case have to be supported out of some fund of public money it might be psychologically sounder that the help came from the funds of the Ministry of Pensions. He asked whether the Special Appeals Tribunal to re-examine old cases in the light of new principles was still in being.

Mr. W. KEENAN instanced the case of a man with over 18 years' service in the Army who died from coronary thrombosis and whose widow had approached him about a pension. When he opened the case before the Tribunal he was told that the opinion expressed by the Ministry's medical adviser decided the case even before the Tribunal had looked at it. He was advised that some of the medical authorities on whom he had relied were not necessarily right in asserting that stress, strain, and climatic conditions had anything to do with the onset of coronary thrombosis. The Ministry's view had not altered over the years, but he believed that medical opinion had softened and changed considerably, and he thought that the time had come for second thoughts about pensions in these cases.

Squadron-Leader H. E. COOPER criticized the slowness of the Ministry in settling some of these cases while a man's family suffered. He appealed for a rise in the pension paid for amputations, which was the same as it was in 1919, while the cost of living has risen out of all proportion.

Preparing an Appeal

Mr. F. ANDERSON suggested that in many of these cases it was worth getting additional information about the case. It might be that there was some contributory cause in a man's service which was not mentioned on the précis sheet before the Tribunal, and he had also found a lot of information in the précis which was foreign to the man concerned. He felt that the applicant should have better facilities to get independent opinions from specialists so that they would be on more equal terms with the Medical Services Division of the Ministry. He sometimes feared, too, that the medical men on the Appeals Tribunal might be far from up-to-date in their medical knowledge.

Mr. G. A. ISAACS, making his first speech as Minister of Pensions, apologized for not being able to answer all the questions raised, because he was so new to the job. The proportion of disabled men employed by the Government was considerably over 5%, although the legal responsibility was only 3%. He would do all he could to maintain the standard of humanity set by his predecessors at the Ministry of Pensions and he would carefully consider every point that the debate had brought out.

Swiss Beds for British Patients

Mr. HENDERSON STEWART asked on January 23 for a report on arrangements made to secure places in Swiss sanatoria for Scottish patients with tuberculosis.

Miss M. HERBISON said Mr. McNeil was satisfied, after a visit of inquiry by clinical experts (see *Journal*, December 9, 1950, p. 1342), that a number of beds were available and suitable in Swiss sanatoria. Legislation would be necessary to permit their use under the N.H.S., and the financial implications were now being considered in consultation with Mr. Gaitskell.

Beds for Acute Cases

Mrs. ELIZABETH BRADDOCK asked on January 25 for the number of deaths in Liverpool for the week ending January 13, 1951; how many were over 65 years of age; and what was the number of deaths in Liverpool for the worst of the influenza epidemic in 1919.

Mr. HILARY MARQUAND said there were 949 deaths from all causes. Of the 216 deaths for which influenza was mentioned on the death certificate, 146 were of people aged 65 and over. The greatest number of deaths from all causes in Liverpool in one week during the influenza epidemic in 1919 was 642.

Mrs. BRADDOCK inquired whether the Minister knew the concern in Liverpool at the inability to obtain hospital beds for acutely ill persons, especially aged persons; and what steps he was taking in the matter.

Mr. MARQUAND said that even during the recent heavy pressure 92% of urgent cases had been admitted within 24 hours through the Emergency Bed Bureau, and half the remainder within a day or two. Hospitals had met the situation by restricting admissions of other cases and by early discharge where possible.

Mrs. BRADDOCK further asked if the Minister would ensure that cases were not refused by any hospital while there were empty beds available.

Mr. MARQUAND replied that admissions to hospital must be locally controlled. He added that he had no reason to think that hospitals were refusing to admit patients for whom beds could be made available.

Mr. IAIN MACLEOD suggested that the trouble was in part due to the absence of a statutory undertaking on hospitals to admit the acute sick. Previously this obligation had existed from 1601 to 1948.

Tonsils

On January 25 Mr. W. A. STEWARD asked whether Mr. Marquand knew of cases where patients requiring their tonsils removed had been informed by a number of hospitals that they would have to wait two years.

Mr. MARQUAND answered that the waiting period varied in different areas, and in some had been increased by the need to suspend operations while poliomyelitis was present. So far as resources permitted, additional units and operating sessions were provided.

Universities and Colleges

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

Dr. Alexander Slessor will deliver the James Watson Prize Lecture in the Hall of the Faculty (242, St. Vincent Street, Glasgow) on Wednesday, February 7, at 5 p.m. His subject is "The Role of the Adrenal Cortical Hormones in Diuresis." All medical practitioners are invited to attend the lecture.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the **week ending** January 13. (No. 2).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included) (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending January 13					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	30	5	9	1	5	81	8	18	2	5	1,006	459	81
Deaths	—	—	—	1	—	1	—	—	—	—			
Dysentery	698	65	124	2	1	154	18	44	—	—	344	128	70
Deaths		—		—					—	—			
Encephalitis, acute	2	—	—	—		5	1	1	—	—	5	2	—
Deaths		—			—		—						
Erysipelas			41	8	16			29	5	12			
Food-poisoning	65	22		1		55	14		—				
Infective enteritis or diarrhoea under 2 years				7	14				7	20			
Deaths	18		5	1	—	26		5	3	2			
Measles*	18,658	2,425	355	89	155	2,318	54	48	218	87	12,379	3,304	557
Deaths		1	—	—	—			—	—	—			
Meningococcal infection	61	4	29	7	3	41	1	23	—	1	178	56	28
Deaths		2	—				1	—					
Ophthalmia neonatorum	19	1	9	—		27	2	7	—	—	87	61	27
Pneumonia, influenzal	2,538	160	111	75	4	991	79	22	7	7	1,445	1,208	787
Deaths (from influenza)†	890	81	58	38	2	47	8	6	—	2			
Pneumonia, primary			694					439					
Deaths	982	125		51	17	300	49		11	13			
Poliomyelitis, acute:													
Paralytic	27	—	} 2	} 1	} 5	} 50	} 5	} 1	}—	} 4	} 50	} 11	} 6
Non-paralytic	11	1											
Deaths§	6	—			—	9	—						
Puerperal fever			5				—	10	—				
Puerperal pyrexia‖	102	13	4	3		70	6	9	2	1	162	142	70
Scarlet fever	852	70	219	37	57	1,758	92	261	162	62	1,963	1,355	989
Deaths		—	—	—	—			—	—	—			
Smallpox	11	—	—	—		—	—	—	—	—			
Deaths				—					—	—			
(1) Tuberculosis, respiratory			116	33				130	41				
(2) Tuberculosis, non-respiratory			17	1				31	4				
(1) Deaths	} 256	{ 44	34	11	11	} 214	{ 24	35	7	18			
(2) Deaths		2	2	—	1		1	5	—	1			
Typhoid fever	—	—	1	1	—	8	—	1	—	—			
Deaths¶	—	—	—	—		1	—	—	—	—			
Paratyphoid fever	8	1	2 (B)	—		—	—	—	—	—	31	8	5
Whooping-cough	4,980	490	882	61	79	1,535	59	359	67	50	2,825	1,678	1,190
Deaths	15	3	6	—	1	4	—	—	—	—			
Deaths (0–1 year)	326	47	69	16	15	294	40	43	15	25	533	437	294
Deaths (excluding stillbirths)	10,328	1,558	1,202	346	275	5,520	916	652	138	225	6,857	5,983	5,246
Annual death rate (per 1,000 persons living)			24·1					13·1					
Live births	7,109	1,214	894	210	384	7,201	1,142	915	229	385	9,825	7,201	4,942
Annual rate per 1,000 persons living			18·0					18·4					
Stillbirths	186	17	30			191	23	22			271	212	179
Rate per 1,000 total births (including stillborn)			32					23					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Vital Statistics

Influenza

The outstanding features of the statistics for England and Wales for the week ending January 20 are:

(*a*) A material retardation in the rate of increase in influenza deaths (viz., 1,099, compared with 890 in the previous week)—a rate responsible for the biggest increment in such deaths since 1919.

(*b*) A decided decrease in the influenza death rate in the northern region and a slight decrease in the north-western. On the other hand there were material increases in all the other regions, though not approaching the high figures previously reached in the north and north-west.

(*c*) A continued limitation of influenza deaths very much to the older age groups—86% over the age of 55 years.

(*d*) A comparatively small increase in pneumonia cases in England and Wales as a whole and in the great towns.

(*e*) In general a decided and continued limitation of the large numbers of combined influenza and pneumonia deaths to the more northern towns. Greater London, however, gave high figures and a small increase compared with the preceding week.

(*f*) There was an increase in first claims on the National Health Insurance in the week ending January 16 to 426,899 from 412,171 for the whole country. The increase was fairly generally distributed except in the north, north-west, and the London regions, in which there were decreases.

News has been received of an outbreak in Turkey, while Northern Italy is also affected. Information is not yet available about the strains of virus responsible. There has been a recurrence of the influenza outbreak in Sardinia which was attributed to virus B. In Norway in the month of November 27,089 cases of influenza were reported. In Oslo in the week ended December 23, 1950, there were 488 cases. Later there were decreases in weekly figures to 138 and 163, but in the week ended January 13 a slight increase to 212. There was a prevalence of influenza in various of the South Pacific island groups in November, but late information is not available.

Although absenteeism on account of sickness is marked in a number of areas, there is nothing of any particular significance in removals to hospital either in general or for influenza in particular in the week ended January 27.

The following cases of and deaths from pneumonia and influenza in the great towns have been reported:

	18/11	25/11	2/12	9/12	16/12	23/12	30/12	6/1	13/1	20/1
Pneumonia:										
Cases ..	313	302	282	347	374	364	502	956	1,300	1,455
Deaths ..	188	207	198	236	289	351	383	770	982	843
Influenza:										
Deaths ..	16	24	28	34	33	54	102	458	890	1,099

Totals from the first week of the year in the great towns compared with the preceding two years are as follows:

	1949	1950	1951
Pneumonia:			
Cases	1,755	1,676	3,711
Deaths	1,113	832	2,599
Influenza:			
Deaths	132	138	2,443

The following Table shows notifications of pneumonia—primary and influenzal—in England and Wales:

	18/11	25/11	2/12	9/12	16/12	23/12	30/12	6/1	13/1	20/1
Pneumonia	558	490	497	573	684	647	962	1,774	2,538	3,047
Corresponding week, 1949–50	667	710	715	734	676	634	842	1,120	991	890

The deaths cannot be related to the cases in these Tables.

Regional totals of influenza deaths in the great towns in the week ending January 20 and rates per million (in parentheses) were: Northern 74 (59.7), East and West Ridings 74 (31.9), North-western 477 (132.1), North Midland 32 (30.5), Midland 108 (47.0), Eastern 33 (43.9), London and South-eastern 208 (29.6), Southern 23 (27.9), South-western 40 (41.5), Wales 30 (45.2).

Influenza deaths in the great towns by age groups were: under 1, 11; 1–15, 4; 15–25, 8; 25–35, 9; 35–45, 27, 45–55, 90; 55–65, 182; 65–75, 335; 75 and over, 433; all ages, 1,099.

Incidence per million of influenza deaths in the regions compared with the previous week is:

	Week Ending January 13	Week Ending January 20
Northern	91 per million	59.7 per million
North-western	138 „ „	132.1 „ „
London and S.E. ..	21 „ „	29.6 „ „
Remaining regions average	13 „ „	38.3 „ „

The following Table shows the great towns with the largest numbers of influenza and pneumonia deaths for the week ending January 20:

	Total Deaths	Deaths from (*a*) Influenza	Deaths from (*b*) Pneumonia	Deaths from (*a*) and (*b*)
Middlesbrough ..	79	13	8	21
Newcastle ..	140	7	16	23
Sunderland ..	83	11	10	21
Leeds	243	23	31	54
Sheffield	204	8	12	20
Birkenhead ..	120	23	11	34
Blackpool ..	136	29	16	45
Bolton	105	22	11	33
Liverpool ..	631	145	125	270
Manchester ..	396	45	44	89
Preston	75	16	9	25
St. Helens ..	62	23	4	27
Southport ..	58	18	6	24
Wallasey	93	46	12	58
Wigan	81	25	5	30
Birmingham ..	397	25	18	43
Stoke-on-Trent ..	129	14	9	23
Walsall	70	25	7	32
Greater London ..	3,228	252	258	510
Bristol	201	15	22	37
Cardiff	112	14	8	22
Edinburgh ..	241	17	23	40
Glasgow	550	51	38	89
Belfast	309	61	47	108
Dublin	269	20	32	52

Influenza in the Great Towns

The mortality from influenza in the great towns during the first two weeks of this year was mainly concentrated in the north-west of the country. The towns there contributed 50% and 56% of the deaths in the first and second weeks respectively. The returns for the third week show that the number of deaths has declined in the regions where the epidemic began, and the outbreak has apparently moved south. The towns in the Midland region and London had a large increase in mortality during the third week. The returns for the first three weeks are:

Region	No. of Deaths		
	1st Week	2nd Week	3rd Week
Northern	103	113	74
East and West Riding ..	6	34	74
North-West	230	497	477
N. Midland	8	16	32
Midland	11	34	108
East	9	20	33
London and S.E. ..	76	146	208
South	4	12	23
South-West	8	14	40
Wales	3	4	30
Totals	458	890	1,099

Smallpox at Brighton

During the week ending at noon on January 30 no new case of smallpox was notified in Brighton. All contacts are now out of surveillance. Cases coming from outside the Brighton area, who have been under observation in hospital, have proved not to be smallpox. The disease has, throughout, been confined to the Brighton area. The

clinical and laboratory findings in all patients admitted to hospital during the outbreak have now been received. As a result it is accepted that there have been, to date, 29 cases of smallpox. Of these, 10 have died. The date of removal to isolation of the last confirmed case was January 22.

The history of the outbreak was as follows. Smallpox was introduced into this country by an R.A.F. officer, who flew from Karachi by way of Malta. He landed at Leuchars, Fifeshire, and from there travelled to Brighton on November 29, 1950. For the next 12 days he resided in the town. At the beginning of this spell he did not feel well, although medical opinion was doubtful about the cause. It was later proved that this illness was smallpox in a highly modified form.

This original patient infected a young woman in the same Brighton house, and she was in Bevendean Hospital, misdiagnosed, for 10 days. It was only when her father was admitted, seriously ill, on December 27, that smallpox was suspected. Diagnosis was confirmed on December 28. This delay in diagnosis allowed the spread of infection in three foci:

(*a*) The hospital. Here the following contracted the disease: 9 nurses, of whom 3 died; 2 domestics, who both died; 1 gardener, who died; and 1 baby patient, who recovered.

(*b*) A telephone exchange. The second case was employed here, and, as a result, 2 other women were infected.

(*c*) A laundry. The clothes of the original case were sent here, and this led to 6 employees contracting the disease, of whom 2 died.

Outside these 3 main foci there were 5 cases, with 1 death. No definite linkage of infection could be found in 4 of these, but the fifth was a contact of one of the hospital nurses who died of the disease. All cases of smallpox were resident in the Brighton area, and cases reported outside during the outbreak were not confirmed. The vaccinal state of the cases is shown in the Table below.

Case No.	Age	Sex	Date of Rash	Date of Removal to S.P. Hospital	Vaccination State	
					Before Exposure	After Exposure to smallpox Infection
1	34	M	3/12/50	28/12/50	Infancy, 1943, 1949	—
2	25	F	14/12/50	28/12/50	Infancy	—
3*	53	M	23/12/50	28/12/50	,,	—
4	31	F	26/12/50	28/12/50	,,	—
5	63	F	29/12/50	30/12/50	,,	—
6*	28	F	30/12/50	30/12/50	Unvaccinated	29/12/50
7*	28	F	31/12/50	31/12/50	,,	30/12/50
8*	17	F	31/12/50	31/12/50	,,	28/12/50
9	23	F	31/12/50	31/12/50	Infancy	—
10	28	F	2/1/51	2/1/51	,, 1935	28/12/50
11*	38	F	2/1/51	2/1/51	Unvaccinated	29/12/50
12	24	F	2/1/51	2/1/51	,,	30/12/50
13*	43	F	2/1/51	2/1/51	,,	29/12/50
14*	53	F	4/1/51	4/1/51	Infancy	1/1/51 (no take)
15	47	F	6/1/51	6/1/51	,,	30/12/50
16	27	F	8/1/51	8/1/51	Unvaccinated	9/1/51
17	21	F	9/1/51	9/1/51	,,	30/12/50
18	19	F	10/1/51	10/1/51	,,	28/12/50
19	19	F	10/1/51	10/1/51	,,	28/12/50
20*	48	F	10/1/51	10/1/51	,,	29/12/50
21	9	M	9/1/51	9/1/51	,,	30/12/50
22*	20	M	10/1/51	11/1/51	,,	—
23*	54	M	12/1/51	12/1/51	Infancy	29/12/50 (no take)
24	24	F	11/1/51	11/1/51	Unvaccinated	29/12/50
25	21	F	12/1/51	12/1/51	Infancy	28/12/50
26	1	M	9/1/51	10/1/51	Unvaccinated	29/12/50
27	40	F	12/1/51	12/1/51	,,	28/12/50 (no take)
28	6	M	21/1/51	21/1/51	,,	10/1/51
29	18	M	22/1/51	22/1/51	,,	10/1/51

* These patients died.

Suspected Smallpox at Brixham

On the morning of January 30 a woman aged 52 with a rash was admitted to Upton Pine Hospital, Exeter, for diagnosis. She had visited Brighton on January 13–17 and was vaccinated on January 16. Her removal to isolation and the vaccination of contacts are precautionary.

Poliomyelitis

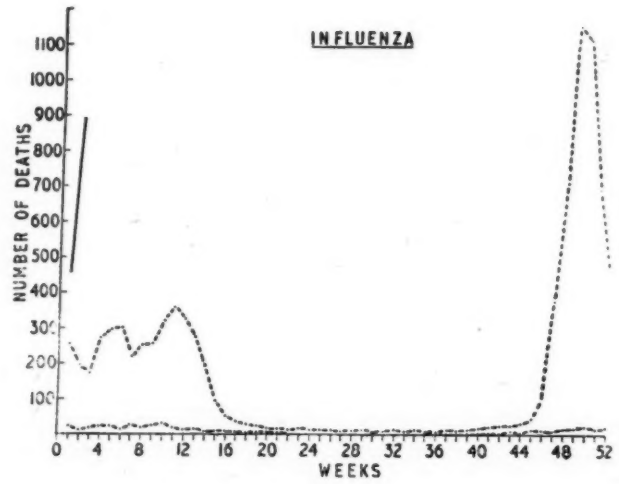
Notifications in the week ending January 20 were: paralytic, 29 (27); non-paralytic, 7 (11); total, 36 (38). Figures for the previous week are in parentheses. Notifications in the weeks named in 1951 and the preceding four years are given in the following table:

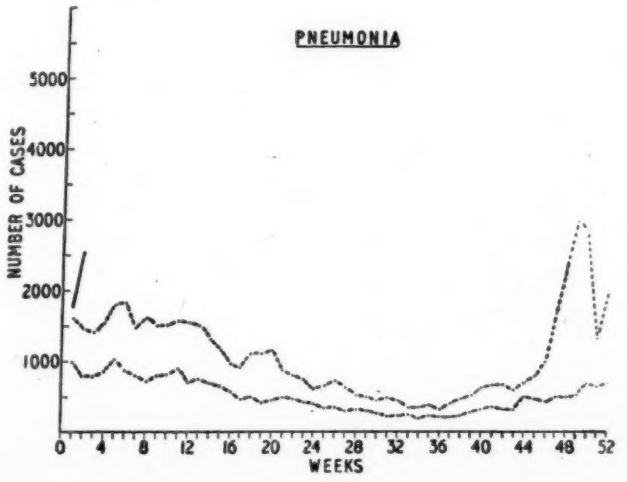
	1947	1948	1949	1950	1951
1st week ..	10	58	20	54	47
2nd week ..	16	49	37	50	38
3rd week ..	10	38	28	51	36
Totals ..	36	145	85	155	121

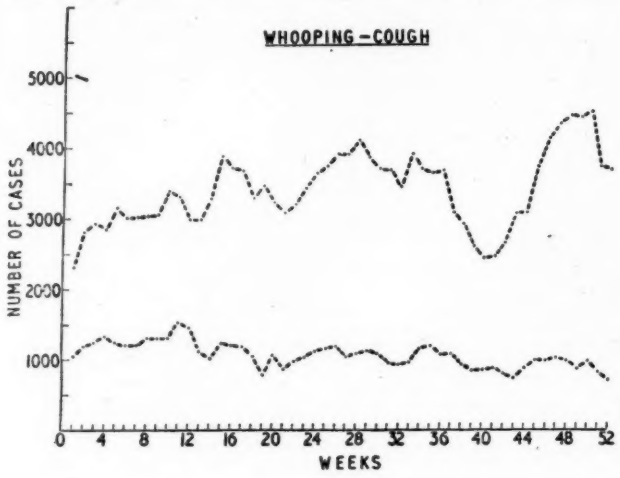
Total notifications for the first three weeks of 1951, following an epidemic year, are therefore materially less than for the same period in the years 1948 and 1950, which followed very high incidence of the disease in 1947 and 1949.

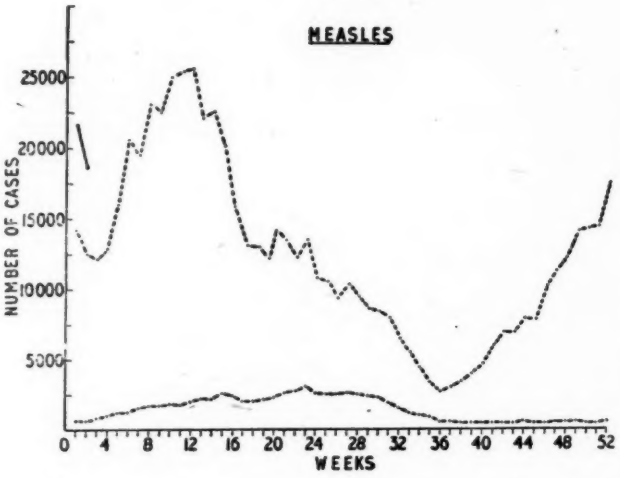
Graphs of Infectious Diseases

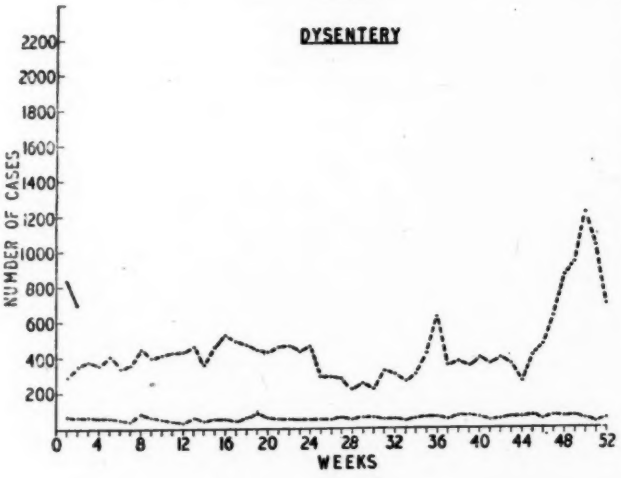
The graphs below show the uncorrected numbers of cases (deaths from influenza) of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus --------, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.











Infectious Diseases

The chief variations in the numbers of notifications of infectious diseases in England and Wales during the week ending January 13 were decreases for measles 3,030, dysentery 136, and scarlet fever 71, and an increase of 764 for acute pneumonia. The largest declines in the incidence of measles were Yorkshire West Riding 762, Lancashire 348, London 328; the only large exception to the general decline was an increase of 86 in Staffordshire. A rise in the incidence of acute pneumonia was fairly general throughout the country, and was especially steep in two areas. The largest increases were in the adjacent counties of Lancashire 233, Cheshire 113, and Yorkshire West Riding 61, and in London 51 and Middlesex 49. The notifications of acute poliomyelitis were 9 fewer than in the preceding week, the largest return being 4 in Surrey. In Scotland the notifications of whooping-cough were doubled during the week.

The notifications of diphtheria in England and Wales (30) were the lowest ever recorded in any week. The largest returns were London 5 and Lancashire 5.

Dysentery

Dysentery was less prevalent throughout the country in the week ending January 13, but the incidence was still very high. The largest returns were: Leicestershire 110 (Leicester C.B. 88, Barrow upon Soar R.D. 13); Yorkshire West Riding 81 (Saddleworth U.D. 26, Sheffield C.B. 12); Lancashire 74 (Oldham C.B. 13, Southport C.B. 11); London 65 (Finsbury 20); Staffordshire 40 (Stoke-on-Trent C.B. 13, Cannock U.D. 13); Middlesex 39 (Enfield U.D. 18); Cheshire 28 (Nantwich R.D. 17); Essex 26; Suffolk 22 (Ipswich C.B. 21); Sussex 21 (Eastbourne C.B. 18); Warwickshire 17 (Birmingham C.B. 12); Surrey 16; Shropshire 16; Durham 14; Glamorganshire 14; Southampton 11; Monmouthshire 11.

Week Ending January 20

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,009, whooping-cough 4,811, diphtheria 42, measles 15,979, acute pneumonia 3,047, acute poliomyelitis 36, dysentery 727, paratyphoid fever 2, typhoid fever 4, smallpox 3. In the great towns 1,099 deaths were attributed to influenza.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accident in the course of their employment were reported in December, 1950, was 116, compared with 155 (revised figure) in November, 1950, and 134 in December, 1949 (*Ministry of Labour Gazette*, January, 1951). There were 24 deaths underground in coal mines reported in December, 1950. The following cases of industrial disease in the United Kingdom were reported during December: lead poisoning, 18; chronic benzene poisoning, 1; compressed-air illness, 1; anthrax, 3; epitheliomatous ulceration, 7 (pitch 5, and oil 2); chrome ulceration, 10; total 40.

During 1950, 1,568 deaths were reported of workpeople (other than seamen) in the course of their employment in the United Kingdom. Of these, 546 occurred at mines and quarries, 816 at factories and other places covered by the Factories Act, and 206 in the railway service. There were 448 deaths underground in coal mines.

During the year the following industrial diseases were reported: lead poisoning, 57; other poisoning, 57; anthrax, 37; epitheliomatous ulceration, 199; chrome ulceration, 143; total, 493.

Medical News

British Surgical Team for Yugoslavia

A British surgical team, led by Mr. C. Price Thomas, surgeon to Westminster and Brompton hospitals, left London on January 27 to visit Yugoslavia for two weeks at the request of the Yugoslav Government to lecture on and give practical demonstrations of the surgical treatment of tuberculosis. The visit is sponsored by the B.M.A. and the British Council. The other members of the team are Dr. Robert Machray, anaesthetist at Westminster and Brompton hospitals, and Mr. Peter Jones, registrar at Brompton Hospital, who will be responsible for post-operational care. The necessary drugs and complete surgical equipment down to the smallest detail have been sent in advance to Belgrade, where the first demonstrations will be given. The team will also go to Zagreb and to Golnik, near Sarajevo, the biggest centre for the treatment of tuberculosis in Yugoslavia.

Liddle Triennial Prize

The subject of the Liddle Triennial Prize, the value of which is £120, is "The Effects of Hormones on the Reaction of the Tissues to Injury." Full particulars may be obtained from the secretary of the London Hospital Medical College, Turner Street, London, E.1, to whom essays for the prize must be sent by July 31, 1952.

Essay Competition for G.P.s

The subject for the Hunterian Society's gold medal for 1951 is "The Treatment of Asthma in General Practice." The competition is open to all general practitioners. Further details may be had from the honorary secretary, Mr. Clement Francis, 75, Wimpole Street, London, W.1.

In Brief

Miss Florence Horsbrugh, M.P., has been appointed a member of the General Medical Council to represent Scotland.

The Irish Gerontological Society was founded on December 6, 1950, and Professor W. J. E. Jessop elected president, Dr. John F. Fleetwood secretary, and Dr. Paul Holland treasurer. Information concerning the new society may be obtained from the secretary, c/o Department of Physiology, Royal College of Surgeons, Dublin.

COMING EVENTS

Society for the Study of Fertility

The second annual conference will be held at Girton College, Cambridge, on June 20 and 21. Further particulars may be had from the secretary, Dr. G. I. M. Swyer, University College Hospital Medical School, London, W.C.1.

Maternity and Child Welfare

The annual conference on maternity and child welfare will be held by the National Association for Maternity and Child Welfare on June 27–29 at Church House, Westminster, London, S.W.1.

Society for Endocrinology

A symposium on "Endocrinological Aspects of Fertility" will be held at the Meeting House of the Zoological Society, Regent's Park, London, N.W.8, on February 16, at 11 a.m. Those desirous of attending, and who will require lunch and tea, should communicate with Professor C. H. Gray, Department of Chemical Pathology, King's College Hospital, London, S.E.5, not later than February 10.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

●INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, London, W.C.—February 5, 5 p.m., "*The Delinquent Child*," by Dr. D. Carroll.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—February 5, 5.30 p.m., lecture-demonstration by Dr. E. Stengel.

PHARMACEUTICAL SOCIETY OF GREAT BRITAIN, 17, Bloomsbury Square, London, W.C.—February 5, 7.30 p.m., "*The Work of the World Health Organization*," by Dr. W. Aeg. Timmerman (Director, Division of Therapeutic Substances, W.H.O.).

ST. ANDREWS UNIVERSITY.—At Chemistry Department, University College, Dundee, February 5, 7.30 p.m., "*Recent Developments in the Study of Carcinogenesis*," by Professor Alexander Haddow.

Tuesday

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, London, W., February 6, 8 p.m., "*Some Aspects of Adler's Theory of Neurosis*," by Dr. E. Weissmann. Discussion will be opened by Drs. Morris Robb and S. Tischler.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppell Street, London, W.C., February 6, 5.30 p.m., "*Language and Thought*," by Dr. Macdonald Critchley.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—February 6, 5 p.m., "*Reticulosis*," by Dr. J. O. Oliver.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Linco'n's Inn Fields, London, W.C.—February 6, 5 p.m., "*Some Problems Involved in Homotransplantation of Tissues, with Particular Reference to Skin*," Arris and Gale Lecture by Mr. W. J. Dempster.

SOCIETY OF PUBLIC ANALYSTS: PHYSICAL METHODS GROUP.—At 4, Grosvenor Gardens, London, S.W., February 6, 6.30 p.m., 29th ordinary meeting on "*X-ray Analysis*." Papers will be read, to be followed by a discussion.

Wednesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—February 7, 5 p.m., "*Medical Mycology*," lecture-demonstration by Dr. R. W. Riddell.

LONDON UNIVERSITY.—At the School of Pharmacy, 17, Bloomsbury Square, London, W.C., February 7, 5.30 p.m., "*The Isolation, Properties, and Functions of the Vitamins B_{12}*," Special University Lecture in Pharmacy by Dr. E. Lester Smith.

●NATIONAL INSTITUTE OF INDUSTRIAL PSYCHOLOGY.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C., February 7, 6 p.m., "*The Institute's Research Into the Unit of Work*," by Mr. David Cox.

NORTH-EAST LONDON CLINICAL SOCIETY.—At Prince of Wales's General Hospital, London, N., February 7, 8.15 p.m., annual general meeting. "*Dermatology—Yesterday, To-day, and To-morrow*," presidential address by Dr. Brian Russell.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow.—February 7, 5 p.m., "*The Role of the Adrenal Cortical Hormones in Diuresis*," James Watson Prize Lecture by Mr. Alexander Slessor.

SOCIETY OF PUBLIC ANALYSTS.—At Chemical Society, Burlington House, Piccadilly, London, W., February 7, 7 p.m., ordinary meeting. Papers will be read.

Thursday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C., February 8, 5.30 p.m., "*Mind and Matter*," by Dr. Russell Brain.

HARVEIAN SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, London, W.—February 8, 8.15 p.m., discussion: "*The Scope of Manipulative Surgery*," speakers, Dr. J. B. Mennell, Mr. P. N. Cutner, and Dr. Guy Beauchamp.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—February 8, 5 p.m., "*Diseases of the Mucous Membrane of the Mouth*," by Dr. L. Forman.

LONDON UNIVERSITY.—At the School of Pharmacy, 17, Bloomsbury Square, London, W.C., February 8, 5.30 p.m., "*The Isolation, Properties, and Functions of the Vitamins B_{12}*," special university lecture in pharmacy by Dr. E. Lester Smith.

ROYAL ARMY MEDICAL COLLEGE.—At Lecture Theatre, John Islip Street, London, S.W., February 8, 5 p.m., "*The Significance of Psychiatry*," by Brigadier J. R. Rees.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—February 8, (1) 3 p.m., "*Ocular Aspects of Sellar and Suprasellar Lesions*," ophthalmology lecture by Dr. S. P. Meadows; (2) 5 p.m., "*The Place of Radiotherapy in the Treatment of Malignant Disease*," Hunterian Lecture by Professor B. W. Windeyer.

ROYAL MEDICAL SOCIETY.—At Assembly Rooms, Edinburgh, February 8, 8 p.m. until 2 a.m., annual ball.

ROYAL SANITARY INSTITUTE.—At Town Hall, Reading, February 8, 10 a.m., papers: "*Modern Tendencies in the Treatment and Prevention of Mental Illness*," by Dr. W. Ogden; "*Some Factors Which Influence Milk Compositional Quality*," by S. J. Rowland, Ph.D., F.R.I.C.; "*Some Factors Which Influence Milk Quantity*," by F. H. Dodd, B.Sc. Afternoon visits.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—February 8, 4.30 p.m., lecture-demonstration on psychiatry.

TORQUAY AND DISTRICT MEDICAL SOCIETY.—February 8, 8.30 p.m., clinical discussion.

WREXHAM AND DISTRICT CLINICAL SOCIETY.—At Wynnstay Arms Hotel, Wrexham, February 8, 7.30 p.m., "*Medical Aspects of an Atomic Explosion*," by Mr. Patrick Clarkson.

Friday

EDINBURGH UNIVERSITY.—At University New Buildings (Anatomy Lecture Theatre), Teviot Place, Edinburgh, February 9, 5 p.m., "*The Physical Analysis of Events in Muscular Contraction*," Sharpey Schafer Memorial Lecture by Professor A. V. Hill, F.R.S.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—February 9, 5.30 p.m., films: (1) "*Hummelscheim's Operation*"; (2) "*Extraction by Magnet of Intra-ocular Foreign Body*." Lecturer, Mr. P. Jameson Evans. A discussion will follow.

LIVERPOOL PSYCHIATRIC CLUB.—At Upton Hospital, Chester, February 9, 6.30 p.m., "*O_2 and CO_2 Therapy*," demonstration and discussion.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—February 9, 8 p.m., "*Sleep*," dissertation by Mr. P. A. Hood.

UNIVERSITY COLLEGE (Physiology Theatre), Gower Street, London, W.C.—February 9, 5.15 p.m., "*Cell Metabolism and Chemotherapeutic Activity*," by Mr. T. S. Work, Ph.D.

APPOINTMENTS

Dr. C. H. St. John has been reappointed a Member, and Dr. A. S. Cato appointed a Member, of the Legislative Council of the Island of Barbados.

CUMMINS, C. F. A., F.R.C.S.Ed., Senior Surgical Registrar to Thoracic Surgical Unit, Papworth Hospital, East Anglian Regional Hospital Board.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Part-time Senior Registrars to Department of Dermatology*, C. D. Calnan, M.B., M.R.C.P., R. H. Meara, M.B., M.R.C.P.; *House-surgeon (Senior House Officer Grade)*, P. G. Jones, F.R.C.S.; *House-physicians (Senior House Officer Grade)*, J. C. Haworth, M.B., Ch.B., D.C.H., F. S. Carter, M.D., M.R.C.P., D.C.H.

LIVERPOOL REGIONAL HOSPITAL BOARD.—The following appointments at the institutions indicated in parentheses are announced: *Whole-time Assistant Psychiatrist*, A. W. H. Smith, M.R.C.S., L.R.C.P., D.P.M. (Rainhill Hospital); *Whole-time Assistant Radiotherapist*, K. Lal, M.B., B.S., D.M.R.T. (Liverpool Radium Institute).

OSBORNE, SYDNEY EDWARD, L.M.S.S.A., D.A., Part-time Consultant Anaesthetist, Chichester Group of Hospitals.

RICHARDS, MYRTLE V., M.B., Ch.B., Temporary Assistant Medical Officer of Health to the Isle of Ely County Council.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—*Consulting Pathologist in South Somerset Clinical Area*, E. J. Harries, M.D. *Consulting Radiologist in West Cornwall Clinical Area*, T. A. Bonar Mason, L.R.C.P.&S.Ed., D.M.R. *Area Pathologist in West Cornwall Clinical Area*, T. C. St. C. Morton, C.B., O.B.E., M.D., F.R.C.P., Air Vice-Marshal, R.A.F.

SUNDERLAND, ELAINE MARION, M.B., Ch.B., D.R.C.O.G., Assistant Medical Officer of Health for Maternity and Child Welfare, Northumberland County Council (Blyth Area).

WHILES, W. H., M.R.C.S., L.R.C.P., D.P.M., Part-time Consultant Child Psychiatrist to Child Guidance Services, Dorset, and the County Borough of Bournemouth.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bector.—On January 20, 1951, at Hammersmith Hospital, London, W., to Nirmal, wife of Dr. N. P. Bector, M.R.C.P., D.C.H., a daughter—Indira.

Rutter.—On January 8, 1951, to Mary (formerly Milton), wife of Dr. Frank W. E. Rutter, 89, Corporation Road, Cardiff, a daughter.

Stewart Thomson.—On January 4, 1951, at R.A.F. Hospital, Rinteln, Germany, to Muriel (formerly Ross), wife of Squadron Leader W. M. Stewart Thomson, M.B., Ch.B., a daughter—Barbara.

Tarnesby (Tarnowski).—On January 21, 1951, at 11, St. Ann's Villas, Kensington, London, W., to Eleanor (formerly Ettlinger), L.M.S.S.A., wife of Herman P. Tarnesby, M.B., B.S., D.R.C.O.G., a sister for Ruth—Sylvia Margot Dodette.

Vaughan-Jones.—On January 26, 1951, to Maureen, wife of Mr. Ronald Vaughan-Jones, F.R.C.S.Ed., D.O.M.S., Holmeswood, Clytha Park, Newport, Mon., a brother for Angela and Andrew.

Woodruff.—On January 21, 1951, at the Middlesex Hospital, London, W., to Helen, wife of Dr. A. W. Woodruff, a son.

MARRIAGES

Wolff—Keenan.—On November 17, 1950, at Brompton Oratory, London, Frederick William Wolff, M.B., B.S., to Catherine Bernadette Keenan.

DEATHS

Armstrong.—On January 12, 1951, at 56, Claremont Road, Surbiton, Surrey, Pattison Armstrong, M.D., D.P.H., aged 78.

Aymer.—On January 9, 1951, at Victoria Villa, Stonehaven, Kincardineshire, Charles Aymer, M.B., C.M., J.P.

Brown.—On January 16, 1951, at 511, Gilmerton Road, Edinburgh, George Herbert James Brown, D.S.O., M.B., Ch.B., Lieutenant-Colonel, R.A.M.C., retired.

Clark.—On January 9, 1951, at "Oakdene," 229, Strathmartine Road, Dundee, John Macdonald Clark, M.B., Ch.B., D.A.

Clarke.—On January 7, 1951, at 81, Galgate, Barnard Castle, Co. Durham, Walter Travers Clarke, M.R.C.S., L.R.C.P., late of Morby, Yorks.

Dawes.—On January 4, 1951, at Feckenham, Redditch, Worcs, Edward Peter Dawes, L.R.C.P.&S.Ed., J.P., aged 77.

Dewar.—On January 10, 1951, at the War Memorial Hospital, Burnham-on-Sea, Henry Steele Dewar, M.B., Ch.B., "St. Monans," Dorchester, aged 34.

Ellis.—On January 9, 1951, at "Cartrefle," Aberystwyth, David Ellis, M.D., aged 74.

Ellis.—On January 9, 1951, at Hove, William Charles Ellis, M.D., D.P.H., aged 84.

Fry.—On January 9, 1951, in a nursing-home, Jersey, William Herbert Fry, M.R.C.S., L.R.C.P.

Gurd.—On January 11, 1951, at 5, Cave Hill Road, Belfast, Charles William Gurd, M.B., B.Ch., aged 34.

Hardwicke.—On January 13, 1951, at Worthing, William Perton Allen Hardwicke, L.M.S.S.A., late of Plymouth, aged 77.

Hay.—On January 16, 1951, at Lossiehall, Liff, Angus, David Hill Hay, M.B., Ch.B.

Hayes.—On January 11, 1951, at Hove, Reginald Hewlett Hayes, M.R.C.S., L.R.C.P., late of Cornwall Gardens, London, S.W.

Mason.—On January 10, 1951, at Cockermouth, Mary Emmeline Mason (formerly Joll), M.D., of Cocker Brows, Cockermouth, Cumberland.

Readdie.—On January 10, 1951, Andrew Finlay Readdie, M.C., L.R.C.P.& S.Ed., L.R.F.P.S.Glas., of "Danecourt," Halifax, Yorks, aged 61.

Synge.—On January 10, 1951, at a Dublin nursing home, Rev. Samuel Synge, M.D., of Annamoe, Co. Wicklow, aged 83.

Ware.—On January 11, 1951, at North Lonsdale Nursing Home, John Ware, M.D., of Netherclose, Ireleth, Askam-in-Furness, Lancs, aged 72.

Wilson.—On January 16, 1951, William Wilson, M.B., Ch.B., of Hanover Park, Peckham, London, S.E.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

What is Histoplasmosis?

Q.—*Can you tell me what histoplasmosis is, and how it is contracted and prevented?*

A.—Histoplasmosis is a systemic mycosis caused by the fungus *Histoplasma capsulatum* Darling, 1906. Although widely distributed in the world, the disease is rare in all countries except the United States. Four cases, probably all infected abroad, have been identified in Great Britain.

The fungus invades the cells of the reticulo-endothelial system, which then undergo hyperplasia, forming granulomatous lesions in various organs and tissues, often with haemorrhage, necrosis, or suppuration and ultimate fibrosis. The symptomatology and clinical features are not specific but depend on the organ or tissue chiefly affected, so that the disease may simulate pulmonary tuberculosis, Hodgkin's disease, Addison's disease, Banti's disease, kala-azar, and other conditions. The diagnosis, therefore, cannot be based on the clinical picture but only on the result of an adequate mycological examination. Histoplasmosis is a highly fatal disease, and no form of treatment has hitherto proved effective.

In the central-eastern part of the United States large numbers of people have been found to react to the histoplasmin skin-sensitivity test, and many of the reactors have shown radiological evidence of healed pulmonary lesions. This may indicate the existence of a mild and unrecognized form of the disease, a view which has been supported by the results of recent close investigations on groups of selected reactors.

We have no precise knowledge of the epidemiology of histoplasmosis, but it may be presumed that infection is caused by the spores of *H. capsulatum* vegetating saprophytically in man's environment, and the probable path of entry is the lungs, by inhalation; however, nothing is known of the natural saprophytic life of the fungus. The disease occurs in dogs, cats, rats, skunks, and some other small animals, but the infection, in man or animal, is not transmitted from host to host, so the disease of the animals can play only an indirect part in epidemiology.

Obviously, there is no known means of prevention.

Croup

Q.—*What are the pathology, symptoms, treatment, and aftercare of non-diphtheritic croup?*

A.—Croup was the name originally used for any disease in which the child had "a sharp stridulous voice—resembling the crowing of a cock," as Francis Home stated in 1765. The name croup, therefore, is simply a description of a group of diseases affecting the larynx. Diphtheritic croup was early separated from non-diphtheritic or non-membranous croup. Frederic Still, in *Common Disorders and Diseases of Childhood*, 1909 (Oxford Medical Publications), divided the forms of non-diphtheritic croup into acute laryngitis, laryngitis stridulosa, and laryngismus stridulus, and, because of the excellence and clarity of his account of these disorders, the questioner will find it well worth his while to read the chapter on laryngeal spasm in Still's book.

Laryngismus stridulus is a condition of momentary spasm of the glottis which may affect infants up to the age of 3 years; they make a sudden crowing noise, and may go

black in the face in their effort to breathe. In this country the condition apparently disappeared at the same time as florid rickets, the spasm being due to the tetany which might occur in that disease. Laryngitis stridulosa is also but rarely seen to-day; it occurs in children between the ages of 3 and 8 years, with a sudden onset of dyspnoea and stridor at night. The child appears really ill and may be extremely breathless, but after one or two hours the symptoms gradually disappear and the child falls asleep, to wake up in the morning quite well. It is liable to be recurrent in some children, and seems to be associated with upper respiratory infection, with cold air, and with adenoidal obstruction.

Acute simple laryngitis or laryngo-tracheo-bronchitis is quite a common condition; it is probably due to bacterial infection, frequently but not necessarily pneumococcal. It has been suggested that it may be due primarily to a virus infection, but this has not been proved. In the mildest cases the child has fever, a slight dry cough, and a hoarse voice. A severe attack is accompanied by high fever, hard dry cough, inspiratory stridor, restlessness, and increasing difficulty in breathing; the child is frightened and often cyanosed. Very careful nursing is by far the most important measure of treatment. The child should be propped up in its cot in a warm room with the atmosphere moistened by steam from a kettle; an oxygen tent is sometimes of value, but often the child seems better outside the tent with the steam kettle near. If the breathing and restlessness are unrelieved by any other measure tracheotomy may be required and should not be delayed until the child is exhausted. Chloramphenicol in doses of 50 mg. per lb. (0.45 kg.) of body weight per day, in six-hourly doses for three to four days, is thought to be the most useful drug available. In its absence streptomycin should be given, or in an early and mild case penicillin. It must be emphasized that the child's survival depends more on the skill of the nursing and on the severity of the infection than on any medicaments.

No special measures are required following recovery, provided the home conditions are satisfactory.

Human Risk in Fowl Pest

Q.—*What is done with the eggs and carcasses of poultry slaughtered in this country on account of Newcastle disease (see your annotation on Fowl Pest, "Journal," January 20, p. 131)? Are they put on the market for sale as food?*

A.—The present practice is either to burn the carcasses or to bury them; the carcasses are not sold for food, because they might spread Newcastle disease virus to other flocks of poultry, usually in the swill. The shells of eggs are decontaminated by dipping the eggs in a dilute solution of washing soda. The eggs are then marketed for eating, but are not used for hatching. At the onset of Newcastle disease fowls occasionally lay eggs which are infected inside their shells, but the risk that virus might survive in this way to infect other poultry is so small that it is ignored.

There is no evidence that the ingestion of Newcastle disease virus has any ill effect on human beings.

Cardiac Murmurs in Pregnancy

Q.—*What murmurs can appear in a normal heart during pregnancy, how are they caused, and what is their significance?*

A.—During the greater part of pregnancy the resting cardiac output is increased to about one and a half times normal. This mild hyperkinetic circulatory state intensifies any natural heart murmur, and may bring out any latent organic murmur. Innocent systolic murmurs at apex or base may thus be noticed during pregnancy for the first time. Similarly, murmurs based on organic valve disease may become more obvious during pregnancy. There is no special murmur related to pregnancy.

Digitalis Glycosides and Gangrene

Q.—*Has the modern treatment of heart disease with single glycosides led to an increased incidence of gangrene in these cases?*

A.—No.

Detergents and Dermatitis

Q.—*Do the commonly used detergents give rise to dermatitis? Can they safely be recommended for use in factories?*

A.—Detergents have been used as substitutes for soap in industry and for domestic purposes for at least five years. In this time very few persons have developed skin lesions which could be due to the soap substitute, and in most of these cases the detergent has been used in unusually high concentration and the hands have been soaked for long periods. The effects of such usage are excessive dryness of the skin and sometimes a sensation of pricking. There is no reason to believe that the use of detergents in a factory would result in an increase in the number of cases of industrial dermatitis.

Pathology of Parkinsonism

Q.—*What are the latest views on the pathology of Parkinsonism? What recent literature is there on this subject?*

A.—It is thought that the lesions are situated in the caudate nucleus and putamen (neostriatum), the globus pallidus (paleostriatum), and also in the substantia nigra. There is no evidence of representation of movements or muscles in these nuclei. Skilled acts, according to Denny-Brown, are thought to be carried out by "a setting of the main motor mechanism (bulbo-spinal) by means of a series of extrapyramidal adjustments (posture, direction, compensating movements) and a supply of power by the cortico-spinal tract." In Parkinsonian syndromes the defects are presumed to be due to the failure of the extrapyramidal components in this system.

An excellent review of the subject, including 348 references and dealing with every aspect of it, is to be found in *Diseases of the Basal Ganglia and Subthalamic Nuclei*, 1945, by D. Denny-Brown. This is reprinted as a separate monograph from the *Oxford Loose-leaf Medicine* (Oxford Medical Publications).

Soft Nails

Q.—*Is there any treatment for soft nails? A married woman, aged 40, parous, who enjoys good health but is subject to chilblains, has had soft nails all her life. All her nails offer little more resistance than two sheets of the "Journal" wrapped round the finger and pressed upon. The leading edge splits and the nail flakes.*

A.—It is probable that the soft nails in this case are a congenital abnormality and are not amenable to treatment other than perhaps by reinforcement by painting with varnishes. It may be that a poor peripheral circulation accentuates the dystrophy, and measures to improve the former might be helpful.

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